BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice.

Vol. XXII.—No. 249.] BALTIMORE, NOVEMBER, 1911. [Price, 25 Cents

CONTENTS.

	PAGE
The Medical Paintings of Velasquez. (Illustrated.) By John W. Churchman, M. D.	383
Studies in Glycosuria. I. Ether Glycosuria. By John H. King, M. D., B. S. Chaffee, D. B. Anderson and L. H. Redelings	388
The Effect of Occlusion of the Various Hepatic Vessels Upon the Liver. (Illustrated.) By M. C. Winternitz, M. D.	396
The Teaching of Experimental Pathology and Pathological Physiology to Large Classes. By Richard M. Pearce M. D.	404
A Protest Against the Indiscriminate Use of the Organic Compounds of Silver in Ophthalmic Practice. By Samuel Theobald, M. D.	407
Notes on Jaundice in Pneumonia. By Fletcher McPhedran, M. B.	408
Abdominal Lipectomy. Report of Two Cases. (Illustrated.) By W. F. Shallenberger, M. D.	410
In Memoriam. Dr. Christian Archibald Herter	411
Notes on New Books	412

THE MEDICAL PAINTINGS OF VELASQUEZ.*

By John W. Churchman, M. D.,

Late Resident Surgeon, The Johns Hopkins Hospital.

There is nothing whatever to show that Velasquez felt any particular interest in the tasks of science or in its achievements. He certainly exhibited no feeling for medicine as a profession, or as one of the humanities. The approach of art to science has often been more obvious. Other men, like Leonardo, have made important contributions to each. Not a few—like Keats and Sainte-Beuve—have known, by desertion of the one for the other, the problems and interests of both. Yet Velasquez' mind was of the type which enjoys the dispassionate observation of facts; and in this sense his point of view was at least a new one in art. Vision meant for him, not what it had meant for his predecessors; it meant simply one of the five senses keenly developed and used without fear or favor. Such sympathy with the method of science, despite any indifference to its content, it is not far-fetched to describe as intellectual kinship. In this man, art and science drew near; and the gap between them was further narrowed by the fact that the actual phenomena which fell in Velasquez' way chanced to be the ones with which medicine is herself concerned.

Strange as Velasquez' fascination by oddness and deformity of mind and body were, he was by no means unique in his choice of material which happens to have a medical interest. He was, indeed, quite unique in the extent to which his choice was of this character; but the field of medicine he shares with many other painters. There was Jan Steen, for example, in the Netherlands. Yet sunlight and shadow could hardly present a sharper contrast than did these two men; nor could bar-room, where the one idled away his days, and king's-court, where the other lived out his career. In almost every detail and circumstance of outward life and mental outlook what the one man was the other was not. The Dutchman brought to medical life the methods of pictorial art; his interest in medicine was casual and anecdotal. Velasquez was interested neither in episodes nor in events. He apprehended and constantly maintained the purely objective attitude.

The pictures of Velasquez which possess unusual medical interest, belong to the Dwarf and Jester Group.[1] With three exceptions, they were painted in the last ten years of his life and represent, therefore, his mature work. The earliest of them is the Geographer of the Rouen Gallery. (Fig. 1.)

* Read at the meeting of the Johns Hopkins Hospital Historical Club April 10, 1911.

[1] The two mendicants (Menippus and Aesop) and the Berlin del Borro (of somewhat doubtful authenticity), though allied to this group, should be separately considered.

The subject of this portrait is probably the same person as the one represented in the striking Pablillos de Valladolid (Fig. 2). The Bouffon Pernia (Fig. 3) and the Don Juan of Austria (Fig. 4) complete the Buffoon Group.

The Dwarf pictures fall into two groups according to the predominance of portraiture or pathology. In the first group Velasquez has immortalized those of his dwarfed every-day companions whose deficiencies were only physical. Here belong the El Primo (Fig. 5), the Don Sebastian de Morra (Fig. 6), the Don Antonio d'Ingles (Fig. 7), and the Don Carlos and his Dwarf (Fig. 8). The Don Carlos in the Riding School in the Westminster Collection, includes, in the background two court dwarfs; and mention should be made of the portraits of two fragile, stunted, royal children (Philip Prosper, Royal Gallery, Vienna, and Don Carlos, Wallace Collection, London).

More striking is the group in which the monstrous predominates. These are the pictures it is hardest to imagine a painter producing; yet Velasquez seems to have painted these prodigies "with care and pleasure, just as he would have painted a pretty woman—without a thought." One recalls Charles Morice's remark about Cézanne "A potato is as significant for him as a human face."

The most remarkable of this group is the El Niño de Vallecas (Fig. 9). It has been said that one can hear this idiot dwarf's nasal whine. But in the El Bobo de Coria (Fig. 10), pathology has gained even more complete mastery. All that there is appaling in an idiot face is here. The crossed eyes, the pallor, the pathetic leer—nothing which fidelity of draughtsmanship dictates has been omitted. Somewhat less gruesome is the Idiot of the Vienna Museum (Fig. 11) (called also The Laughing Boy); but its authenticity is not beyond dispute.

In the picture called Las Meniñas (Fig. 12) two dwarfs appear; but so far from dominating the scene they are quite incidental. Maria Barbolo and Nicolasico Pertusato stand in the lower right-hand corner of the painting. The former has a cretinoid face and figure; the latter is a hydrocephalic, his miniature form emphasized by the great dog at his feet. The painting is of royal personages; the royal playthings happen to be of the group.

It certainly was not the fact that Velasquez' career narrowed the material at his disposal and forced this curious choice of subject on him; nor that the life of the world of his day was calculated to shrink his intellectual concerns. Consider, for a moment, the world in which he lived; and see if you would expect it to inspire a painter to devote his talents to dwarfs and fools. It was a world in which kingdoms were being daily destroyed, thrones reoccupied over night, territorial boundaries readjusted with every swing of the pendulum, armies slaughtered like rats, undreamed of countries explored, traditions ruthlessly set aside. Not many years before Velasquez' birth Copernicus and Columbus had created a new heaven and a new earth; and his life-time was pitched in that period of novelty and enthusiasm and intellectual adventure which has given us our own heritage of emancipation and at which we have never ceased to marvel. Erasmus, Savonarola, Melanchthon and Sir Thomas More had not long been dead; Zwingli, Knox, Calvin and Loyola were names fresh in memory and potent in influence; and the mantle of leadership had fallen on a host of Velasquez' contemporaries, all of them names for all time: Corneille, Racine, Molière, Descartes, Locke, Spinoza, Leibnitz, Milton, Bunyan, Pope, Swift, Dryden, Addison, Newton and Harvey. Not content with this exhibition of stars the managers of the political show had prepared a monster carnival of intrigue and slaughter in which Tilly, Wallenstein, Gustavus Adolphus, Cromwell, Richelieu, Mazarin and a host of others were taking part. Europe was a-drip with blood; bivouacs were never quenched; every rising sun greeted a fresh hero of carnage and adventure. It is a task merely to list the events which brought about the separation of the Teutonic nations from Rome, and the transfer of progress from Italy and Spain to England and Holland. The pace had begun to tell, it is true, on Velasquez' own country; but though Spain was being now distanced she had recently known, and was still knowing, glorious times. Only 80 years before the painter's birth Don Carlos I of Spain had inherited the rule over more extensive dominions than any since the days of Charlemagne; and the fortunes of Spain had by no means waned when this extensively landed gentleman was chosen by the electors of Germany as Charles V of the Holy Roman Empire. In the life-time of Velasquez' parents Spain was in her hey-day; and the painter was born to an unexcelled heritage of national romance and honor and pride. He was destined, it is true, to see that heritage threatened; for, during his life-time, Spain and Italy—hitherto in the van of progress—began, like boys at the tag end of a parade, to lose interest in the line of march and wander up side alleys. The decadence was rapid. Spain, thanks to her king's conservative intellectual policy, failed to keep step with civilization; and not a great deal of water had flowed under the bridge before she had reached the level of a third-rate power. It is not without significance that, in the early days of her decadence, she should have produced one of the most progressive minds in all art; and that the spirit which, elsewhere in Europe, was touching science with a new life, should have singled out in Spain not a natural philosopher, but a painter. No one would, of course, for a moment expect European events—of no matter what magnitude—to have any *direct* influence on the artistic material chosen by a man like Velasquez. Court painter though he was, there was never any danger that he become an artist of the Washington-Crossing-the-Delaware type; he was immune to what has been so well called the anecdotal blight of the once-upon-a-time school. The exciting drama of European history did not disturb him in his studio; and it is not strange that this is so. But the drama was enacting, none the less; and Velasquez' choice of sordid material was forced on him by no lack of splendid show in the world without.

It must be remembered, too, that Velasquez by no means lived in obscurity. He became a part—in the end, a somewhat important part—of the distinguished and influential

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

life of Spain: and his career, from the first, lacked neither variety nor distinction. He was not even of humble parentage and Seville—the city of his birth—was the glory of the Spanish realms. His father, though poor, traced his ancestry through a Portuguese house to the kings of Alba Longa: and his Sevillan mother, whose name the son has immortalized, belonged to the hidalgas. His early advance was rapid. At 23—backed by influence—he had made for himself a secure place in Madrid; had painted the king's portrait; had been appointed court painter; and had been given a studio in the palace and a residence in the city. Painters were indeed in these days none too highly respected;[2] but Velasquez' position in Madrid gave him an opportunity for contact with men of distinction in the various walks of life. In 1628, for instance, he had the rare chance of a nine months' intimacy with Rubens, who had been sent to Spain on a diplomatic mission, but who managed, during his stay, to awaken Velasquez from his artistic lethargy and to persuade him to make the Italian journey.[3] In Rome he must have been a personage of some note: for he lived first at the Vatican, then at the Villa Medici, which was subsequently purchased by Colbert for the French Academy of Painting. He reached Spain again in 1631 and "His Majesty," writes Pacheco, "was greatly pleased at his return." Then followed 18 years of productive work, rewarded by many honors. In 1648 there was a second journey to Italy and, on his return, the appointment as Marshal of the Palace. It was in his capacity as Marshal that arrangements for a royal journey to the Pyrenees[4] fell to his lot, and here he contracted a "subtle, syncopal, tertian fever" of which he died (1660). Honors followed him to his death; and he was attended in his last moments by the Archbishop of Tyre and Patriarch of both Indies. Two years before he had been invested with the Habit of Santiago; but only after a long discussion, during which a council had reported that they "approved his age, purity of blood and lineage, but disapproved the nobility of his paternal and maternal ancestors." A dispensation for defective nobility was then issued by Pope Alexander VI; and Diego de Silva was created "hijo dalgo" by the king's order. The cross of the order of Santiago was conferred, after the artist's death, by order of the king.

[2] When Rubens, then in the full maturity of his powers and at the height of his glory, was sent by Holland to Madrid on a mission relating to the conclusion of peace between Spain and England, the Spanish king wrote, complaining that "such important matters should be confided to a painter . . . . , to a man of such an inferior position."

[3] It is interesting and significant that Velasquez escaped, in the words of de Beruete, being "seduced by the magic conceptions of Rubens." There is said to be one picture (a portrait of Philip IV on horseback in the Imperial Gallery of the Grand Duke of Tuscany in Florence) which was at first attributed to Rubens, but is now supposed to have been painted by Velasquez as a model for the Taccas bronze statue at Madrid. I know of no other painting about which similar confusion could possibly exist.

[4] The journey was made to celebrate the Treaty of the Pyrenees (ending a war waged by Mazarin against Spain) and the betrothal of the Infanta Maria Theresa to Louis XIV of France.

Honor, then, was his in abundance; and his life among men of distinction, both at the court and on his European journeys, was hardly one to contract his intellectual interests. This is, however, not quite the whole story, for in spite of the influential position which Velasquez early obtained at the Spanish court, it was among the court underlings that many of his days were spent. In the court registers he appears among the dwarfs, jesters and barbers of the palace. As late as 1637 a list was published containing the names of dwarfs, jesters, musicians, barbers, etc., to whom were given clothes of grace. Here one reads "the clothes of the barbers and of Diego Velazquez may be reduced to 80 Ducats, and those of the officials of the wardrobe to 70."[5] In the list of places assigned to the spectators of a bull fight (1642), Velasquez is put in the fourth tier with the servants of the grandees, the barbers of the palace and other underlings. During the painter's trip through Italy the Ambassador at Madrid wrote to the Archbishop of Pisa, à propos of a visit Velasquez was about to make: "Be careful to say 'you' to him and not 'your excellency'; for after all he is nothing but a painter."

One must, of course, bear in mind the position of relative honor held by dwarfs and jesters in the courts of Velasquez' day. Spain, indeed, rather outdid England and the rest of Europe in this matter; though royal fondness for miniature men was an old and general hobby. In Scandinavian mythology dwarfs originated as maggots in giants; but in actual life their acute and active minds, their sensitive natures, made the maggots and not the giants the choice of kings and queens. Not only were the pygmies royal favorites; some of them were noted characters and a few, able men. Men like Philetus of Cos, Vladislas Cubitas,—King of Poland—and Pepin le bref, though of doll-like physique, were diminutive neither in mind nor in achievement. Strangely enough, however, the royal fancy did not always require an excess of mental endowment to offset the physical deficiencies. Bébé, for instance, the dwarf of Stanislaus of Poland, was practically an idiot; and the pet presented to Henrietta of France in a pie, could hardly have been highly regarded to be so lightly treated. Yet some of Velasquez' miniature associates were undoubtedly attractive and intelligent men. It is interesting to recall that Zuloaga, who has commemorated on canvas the repulsive features of his dwarfed servant, sometimes dreamed of collaborating with a great composer on an opera written about the life and death of that dwarf. "He was my servant," said Zuloaga. "A strange man, very hideous, physically distorted. But his life was wonderful. His death—he died of love."

The buffoons, too (*truhanes* or *hombres de placer*), possessing a sinister power, held a place in court by no means insignificant. "They represented," says Justi, "freedom of speech in its lowest degradation"; and, though employed ostensibly for royal amusements, they became a power by gaining the royal ear. Embassies were not infrequently entrusted to them; and instances are on record of wise men having played the fool in order to have the fool's influence with the

[5] The ducat was worth about 23 cents.

king. "A vaudeville supported by his Catholic Majesty." Beruete has called this group of miniature and clownish men; but Velasquez' classification with them must be interpreted in the light of the place they held in the court life of the time.

His choice of these bizarre types for portraiture is of course not unique in art. Carreño, Rubens, Fortuny, Zamacois and many others have produced pictures of dwarfs. But Velasquez alone has painted a large series of this kind; he alone has entrusted his fate in so large part to so precarious a medium; he alone has introduced such subjects into his best pictures—into the picture, indeed, which, if all else he did perished, would still entitle him to a high place in art. These are sufficiently striking facts. One does not overlook the other work that Velasquez did; but the dwarf and jester group cannot themselves be overlooked, nor regarded as incidental. They form a large, an integral part of his artistic output.

There is no warrant for assuming that Velasquez' peculiar choice of medical material in his art indicated any spirited interest in medicine. Such an interest, if it had existed, would hardly have confined itself to a restricted and revolting clinical field; it might have been expected, as Steen's did, to select some of the more human aspects of medical life—aspects more likely to awaken interest and more certainly suitable to the purposes of art. Spanish medicine was, indeed, in no condition to arouse any vivid enthusiasm. The uprising of the Germanic spirit in the North and the gradual degeneration of the South were giving a new direction to the history of science. Every one is familiar with the galaxy of medical stars flashing in the Netherlands, in England, in France and in Italy; but Spanish names, if they are known to us at all, hardly match those in the list which includes Boerhaave and Harvey. Even during the days of her political supremacy Spain seems to have failed singularly to beget physicians of the very first rank. Lisbon, Salamanca and Alcala produced, of course, medical men of some importance; but, aside from the Belgian-born Vesalius not a single Spaniard achieved immortality in a day when physicians of other European countries were writing their names for all time.[6]

Consider, too, how abruptly Velasquez turned his face on his artistic precedents in painting these pictures. Painting, in contrast with Castillian architecture and literature appeared late and developed slowly in Spain; and it continued to be hemmed in by the straitest conventions. The three schools (of Castille, of Andalusia and of Valencia) differed in many respects, but they were one in their devotional character. The church was the sole patron of art; and most Spanish painters spent a part of, many of them all, their lives in convents and cathedrals. "The chief end of the works of Christian art," wrote Velasquez' own father-in-law, "is to persuade men to piety and to bring them to God." "Even at Alcala and Salamanca," writes Sterling-Maxwell, "St. Jerome was always more popular than Cicero." Yet Velasquez, growing up in this tradition, became the painter of "sinners of the court rather than saints of the calendar."

It is interesting to speculate as to this extraordinary choice of subject on the part of a man of unexcelled powers, who lived in an exciting world—the friend of celebrities, the intimate of kings. Certainly such a man would hardly confine his artistic output to the still life, from which he learned his draughtsmanship; and line the galleries of Europe—as Weenix did—with melons and grapes that might have come from a country fair or with fish and sides of beef to rejoice any butcher's heart. Yet see how he did confine his interests. The insipid Hapsburg face he must, as court painter, reproduce; a task, in itself, not altogether promising, the degenerating Hapsburg kings of Spain being, at this time, in the suburbs of imperial melancholy.[7] Yet Velasquez, when free from this imposed task, did not flee to stirring subjects; he continued, in Beruete's phrase, to "chant a hymn to ugliness"; and after leaving the royal personage, whose features are familiar solely because Velasquez painted them and whose name has small title to remembrance save as the inventor of the *golilla*—a mode in collars—Velasquez goes to the degenerate playthings of this royal degenerate. It seems an obvious suggestion that the painting of these creatures was ordered by their melancholy owner and simply fell in Velasquez' day's work. Yet why did he lavish such care on them; if they repelled him, why did he not—as others had done—introduce them into groups where they could serve as foils for beauty? One is tempted to appeal to the melancholy genius of Spain, to the tendency to brood over the idea of death, which those authorized to speak regard as much more characteristic of the country than the notorious gaiety of southern Europe. Yet it is just this absence of any feeling on the subject, which impresses you strongly. It would be difficult to find a more perfect example of objective painting. Not only, are no distressing details of repulsive objects omitted; but what is much more striking, because much rarer, is the absence of all effort to give a tragic twist to things. The man who painted them might never have had an emotion, and seems indifferent about awakening any. He handled skulls, he fondled them; but never an "Alas, poor Yorick!" escaped his lips. One imagines him gazing at these living abortions with senses alert but with feelings all unstirred. And that, one may say again, is the attitude of science, not of art. No doubt he painted these pictures simply because he wanted to; no doubt, once dwarfs and jesters had aroused his interest, he gave absolutely no thought to their fitness as artistic material. Hidden, refined motives need not be sought for; but intellectual lethargy, said to be an Andalusian trait, is apparent. And that is the interesting light a consideration of this group of pictures throws on the man, marking him off from those who are interested, first,

[6] In the note on Spanish medicine, which is appended, I have indicated some of the important physicians of the time and their achievements. No epoch-making names occur; but it is of interest to see that a few important early contributions were made (note especially the institution of the *Hospital dels folls* at Valencia and the work of Andreas a Laguna in genito-urinary surgery).

[7] One of them (Philip II) on seeing a man laugh, said: "Either that man is mad or he has been reading Don Quixote."

FIG. 5.

FIG. 6.

FIG. 7.

FIG. 8.

FIG. 9.

FIG. 10.

FIG. 11.

FIG. 12.

in having something worthy to paint and only secondarily in painting it. Instead of selecting his material he allowed his material to select him. On opening his eyes in the morning dwarfs and jesters were the things in his field of vision; they satisfied his artistic demands, in which imaginative needs played little part. To their reproduction on canvas he gave a conscientious draughtsmanship and an infinite talent; in selecting them to paint at all he was intellectually indolent to a degree. Mr. Low has recently written of one of his friends: "He was a man (in Gautier's phrase) for whom the visible world really existed; and *therefore* he was inclined to give Velasquez the supreme place in art." Velasquez' visible world was peopled by deformed and clownish men; their existence was real for him; beyond such a world one imagines he seldom looked.

At any rate, the importance of these pictures in the history of art is of the greatest. They began a new era. One of them Giordano called the Theology of Painting; and though there is no agreement as to what he meant, there is general agreement that it was high praise. There are, of course, those now —there have always been those—who feel that the painting of deformed and clownish men is an artistic achievement of about equal value with learning to write with one's toes. Yet high praise—even worship—Velasquez has received from painters of varied temperaments. His voice—a modern voice in mediæval times, a scientific voice in art—has hushed a good deal of talk about beauty as the sole concern of art. He was not without his own artistic convictions. "I would rather," he said to some one who suggested Rubens as a model, "be the first of vulgar than the second of refined painters." He even had a formula ("Truth, not painting") which, though often quoted, may be made to mean whatever you like. Yet it is certain he did not take rules of thumb very seriously. One imagines his sombre face smiling quietly at formulæ. "A picture is a painted poem," said the ancient Chinese; "I celebrate myself and sing myself," shouted Walt Whitman; "Art is simply and solely the effective transmission of experience," writes Tolstoi; "Paint the soul, never mind the arms and legs," was the friar's advice to Fra Lippo Lippi; "There is no excuse for art, unless it present something different from nature," wrote Goethe. There are the formulæ; here are the paintings; and they do not fit. "Painting," Velasquez would probably have replied, in Corot's words, "is not so complicated as you make out"; or in Huysmann's, "I write what I have seen, what I have felt, what I have experienced, and I write it as well as I can, that is all."

Strangely enough, a Spanish poet (Quevedo) has used, in describing Velasquez, the very metaphor—almost the very words—which have come to stand for the Shakesperian attitude in art:

> "Then deem the picture—by the skill,
> That few shall reach and none surpass,
> Delighted and deluded still—
> The face of nature in a glass."

Great divergence of opinion exists as to the exact number of genuine Velasquez paintings extant. Twenty-four pictures, attributed to this artist in the early inventories of the palace, were destroyed in the fire at the Alcazar—among them three portraits of buffoons, descriptions of which (by Palermino) have survived. Beruete credits Velasquez with only 83 original paintings; Curtis describes a much larger number. In addition to the Menippus, Æsop and del Borro and to the portraits of sickly children (Philip Prosper and Don Carlos) there are 19 extant paintings belonging to the series of Jesters, Dwarfs and Idiots. The genuineness of Nos. 2, 5 and 19 is not beyond question; but in the case of the other 16 authenticity has been established.

PAINTINGS BY VELASQUEZ IN WHICH DWARFS, JESTERS AND IDIOTS ARE REPRESENTED.

I. Jesters:
- *1. Pablillos de Valladolid. Prado, Madrid.
- *2. Bouffon (Cristobal de Pernia). Prado, Madrid.
- *3. Don Juan of Austria. Prado, Madrid.
- *4. Portrait du Géographe. Rouen.

II. Dwarfs:
- *5. Antonio d'Ingles. Prado, Madrid.
- *6. El Primo. Prado, Madrid.
- *7. Don Sebastian de Morra. Prado, Madrid.
- *8. Carlos and his Dwarf. Copley Museum, Boston.
- °9. A Dwarf with dog and parrot. Gallery Lord Ashburton.
- °10. Two dwarfs leading a spotted hound. Louvre.
- °11. A Spanish court dwarf. Royal Museum, Berlin.
- 12. Olivares and Balthasar Carlos with dwarfs. Gallery, Duke of Westminster, Grosvenor House.
- °13. A dwarf seated reading. Gallery Señor Salamanca, Madrid.
- °14. Prince Balthasar in riding school (similar to 12). Wallace Gallery.
- *15. Las Meniñas. Prado, Madrid.
- 16. Die Infantin Margarete und die Zwergin. Maria Barbola.

III. Idiots:
- *17. El Niño de Vallecas. Prado, Madrid.
- *18. El Bobo de Coria. Prado, Madrid.
- *19. Der lachende Bursche (or der Idiot). Royal Gallery, Vienna.

Pictures marked * are here reproduced; the mark ° before the title signifies that the gallery stated may not be the present site of the picture in question.

NOTE ON SPANISH MEDICINE IN THE DAYS OF VELASQUEZ.

Though Spanish names of the very first importance are wanting, Spanish physicians and surgeons in the XVI century were sufficiently active to have left their mark on the times. As early as 1545 a treatise on the operation for vesical calculus was in circulation (Juan Gutièrrez); and a number of publications appeared on the treatment of wounds and on trepanation. These treatises were written by the professors at Salamanca, at Seville, at Lisbon, and by the court physicians. One of the important monographs was by Bartholomé de Aguero (1531-1597), professor at Seville, who was a strong exponent of the immediate closure of wounds; in fresh wounds he advocated protection from air and the use of coagulating and drying materials. In Spain, as elsewhere, much energy was devoted to maintaining the traditions and recording the history of medicine; commentaries and translations were numerous; Hippocrates, Galen and Avicenna had their exponents. The author of one of the histories of medicine (Lusitanius of Lisbon) deserves especial mention for

having advanced what is practically the accepted theory of "an epidemical constitution" and "a contagium."

The Spanish Galen (Andreas a Laguna) was an interesting figure of the times. Most of his life was spent at the court of Charles V. He was a physician, philosopher and statesman who lost his life in the plague at Metz. He wrote one of the earliest treatises on the treatment of urethral stricture with bougies. His book entitled "Methodus cognoscendi exstirpandique excrescentes in vesicae collo carunculas" must have been one of the very early works on the subject.

The most interesting figure was, of course, Vesalius. He was born in Brussels and held professorships in Padua, Bologna and Pisa. On the abdication of Charles V, Vesalius, who had accompanied him into Spain, went into the service of Philip II. Here, the court duties, the jealousy of Spanish physicians, the hatred of the clergy and the lack of anatomical material preyed on his melancholy temperament, and he decided to leave Spain and make a crusade to Jerusalem. On the death of Fallopius, he was called to succeed him in the Paduan professorship, but was shipwrecked on the way home and died in hunger and misery.

One of the most important contributions of Spain to mediæval medicine was the establishment of the *Hospital dels folls a:* Valencia. It was here that probably the first effort was made to treat psychopathic patients reasonably and humanely. The hospital was founded in 1409 by Bernardo Andreu, following a mission conducted by the brothers Gilaberto Jafré in the cathedral. According to Lope (*Las Locos de Valencia*) this hospital was a show place and much frequented by visitors.

Other names that should be mentioned are:

Dionista Daça Chacon: Physician to Charles V, Philip II, Don Carlos and Don Juan of Austria: advocated non-poisonous nature of gunshot wounds.

Francisca Lopez: Physician of Charles V. Extracted Avicenna's Kanon.

Vallesius: Professor at Alcala, published explanations of the aphorisms, later quoted by Boerhaave.

Luis de Lemos: Professor at Salamanca; one of the first to make inquiry into the authenticity of the Hippocratic writings.

Roderigo a Castro: Author of an important treatise on gynecology: De universa mulierum medicina opus absolutissimum! 1603.

Mercado: Treatises on typhus, gynecology, obstetrics and children's diseases; famous work on the garrote.

Diaz: Professor at Alcala, known for writings on kidney diseases and the relation of vesical calculus to gout.

Boccangelino: One of the best authors of the XVI century on the plague.

Francisco Valles: One of the earliest pathological anatomists who, with Pedro Ximenes, attempted to elucidate Galens, "De locis affectis," by anatomical work.

DESCRIPTION OF PLATES.

Fig. 1.—"Portrait d'homme dissertant sur une mappemonde." Museum at Rouen. Also known as "Portrait de Cristophe Colomb" and as "Portrait du Géographe." Attributed to Ribera and to Carreño. Supposed by Bonnat and Madrazo to have been retouched by Velasquez many years after it was painted, with Pablillos de Valladolid for a model. "Le mouvement de la main devient tout naturellement un geste de moquerie à l'addresse des navigateurs et de ces découvreurs de terres inconnues qui promènent leur curiosité inquiète autour de la mappemonde, et le rire épanoui du bouffon se gausse de leurs déconvenues." (Louis Gonze: Gazette des Beaux-Arts, 1893.)

Fig. 2.—Pablillos de Valladolid, sometimes called The Comedian. Subject supposed to be the same as that of the Rouen "Portrait du Geographe."

Fig. 3.—Portrait of the Bouffon, Pernia. Prado, Madrid. This portrait is not regarded as a genuine Velasquez by Beruete.

Fig. 4.—Don Juan of Austria, Bouffon of Philip IV, the Prado, Madrid. Don Juan of Austria was a natural son of Charles V. The name was also borne by a bastard son of Philip IV and the actress la Calderona.

Fig. 5.—El Primo. The Prado, Madrid.

Fig. 6.—Don Sebastian de Morra. The Prado, Madrid. The original was injured by fire and many of its details blurred.

Fig. 7.—Portrait of Antonio d'Ingles. The Prado, Madrid. Antonio was the dwarf of Philip IV.

Fig. 8.—Carlos and his Dwarf. Copley Museum, Boston.

Fig. 9.—El Niño de Vallecas. The Prado, Madrid.

Fig. 10.—El Bobo de Coria. The Prado, Madrid.

Fig. 11.—The Laughing Boy. Called also The Idiot. Royal Gallery, Vienna.

Fig. 12.—Las Meniñas. Called by Giordano The Gospel, or Theology of Painting. Las Meniñas were girls who had not yet assumed the womanly heels: they wore neither mantle nor hat and like the pages in France, served their King and Queen. In the center of the picture stands the Infanta Maria Margarita. She is receiving a cup of water from the Queen's handmaid, Doña Maria Augustina Sarmiento. To her left Doña Isabel de Velasco dropping a curtsy. The two dwarfs Maria Barbolo (cretinoid) and Nicolasico Pertusato (hydrocephalic). A woman and a *guardadamas* in mid-background; far back on stairway the Queen's aposentador. In the mirror the reflections of the King and Queen.

STUDIES IN GLYCOSURIA.

I. ETHER GLYCOSURIA.

By John H. King, M. D.,
Associate in Pathology, The Johns Hopkins University
and
B. S. Chaffee, D. B. Anderson and L. H. Redelings.
(From the Hunterian Laboratory of Experimental Pathology, The Johns Hopkins Medical School.)

The first investigator to call attention to the fact that a reducing body may appear in the urine after etherization was Ruschhaupt (1), who observed glycosuria, in two instances, in rabbits under ether. The presence of reducing materials in the urine of dogs following ether anæsthesia was independently observed by Geis and White and P. B. Hawk. Then Seelig (2) undertook a study of the question. In an early paper he drew attention to several interesting results. This author found that ether inhaled for a longer or shorter time caused a marked glycosuria in healthy dogs. The time of appearance

of the sugar was varied. It was found as early as ten minutes after the beginning of the anæsthetic in one case, and as late as two hours in another. In general a reducing body will appear in the urine at the end of one hour if the narcosis is deep.

The quantity of reducing body in the urine can, with little diuresis, amount to 10 per cent, but the average is about 3 or 4 per cent. Seelig thought that the glycosuria increased with the length of the experiment. The glycosuria lasts only a short time. It disappears on an average of about 7 hours after the discontinuance of the anæsthetic, but may last as long as 16 hours or even 24 hours. The glycosuria depends upon a hyperglycæmia, as the sugar in the blood was found increased under the influence of the anæsthetic. The increase in the blood-sugar, however, Seelig points out may not be very striking.

If the glycosuria were dependent upon simple filtration of dextrose through the kidney for its occurrence, then the sugar in the blood should be less after etherization. Such has never been found to be the case, in the author's experiments, nor in ours. Seelig thinks that there might be some participation of the kidney in the process, as he often found albumin in the urine.

After anæsthesia, Seelig states that the glycogen in the liver is less, pointing to this organ as the direct cause of the hyperglycæmia, by increased conversion of glycogen into glucose. He points out some further interesting results which it will be found more advantageous to consider later in our paper. Furthermore, in a second paper, Seelig considers the influence of diet upon the occurrence of this type of glycosuria. Here again it seems preferable to reserve this discussion for later consideration.

Hawk (3) pointed out that during and following ether anæsthesia the urine acquired considerable reducing power, but he did not consider that there occurred a sufficient hyperglycæmia to account for it.

Macleod (4) likewise observed the occurrence of glycosuria under ether, but also regards its influence on the blood-sugar as of very slight extent. The cause, he says, is a mystery. He regards the glycosuria as either due to some permeability of the renal epithelium, or that the anæsthetic may act upon the sugar combination in the blood, increasing the amount of free sugar, which is then immediately filtered off in the urine. A rather interesting point is raised in this paper as to whether the reducing property acquired by the urine is due entirely to dextrose or in part to some other substance. Upon this point our results may throw some light.

Underhill (5) states that ether does not cause any notable change in the sugar content of the blood, when employed in the degree of slight anæsthesia, nor does it induce the passage of a reducing body into the urine though the anæsthesia be prolonged 3-4 hours.

It would seem quite well established that ether, in common with several other drugs, possesses the power of inducing the passage of sugar into the urine.

Experimental.—It seemed desirable before investigating more minutely the mechanism of ether glycosuria to make a few preliminary experiments to confirm its appearance. Accordingly, several dogs were anæsthetized with the ordinary routine ether for anæsthesia. The anæsthesia was deep in every case and the dogs chosen were all healthy active animals. It was found that a very definite reducing property was acquired by the urine after ether anæsthesia.

EXPERIMENT No. 1.—Dog, No. 80. Female. Diet: Meat and bread. Gave 300 cc. of water by stomach tube, 45 minutes before beginning of anæsthesia. Anæsthesia, 10 a. m. to 12 m. Amount of ether given, 150 cc. The urine drawn just prior to beginning of anæsthesia was negative to Fehling's test. At the end of 1 hour, animal was catheterized and 5 cc. of urine obtained. This completely reduced Fehling's solution in a test tube. No. albumin. Catheterized at 3.30 p. m. Urine, 38 cc. Fehling's +. Catheterized at 4.45 p. m. Urine, 35 cc. Fehling's +. June 28, 1910, catheterized at 9 a. m. Urine, 120 cc. Fehling's +.

Remarks.—Ether caused the appearance in the urine of a reducing substance at the end of 1 hour, which persisted for 24 hours.

EXPERIMENT No. 2.—Dog, No. 112. Diet: Meat and bread. Animal was anæsthetized for 5 hours. Urine drawn at end of 20 minutes, after beginning of anæsthesia, reduced Fehling's solution very strongly. Urine drawn by catheter, 36 hours after end of anæsthesia, did not reduce Fehling's solution.

EXPERIMENT No. 3.—Dog, No. 80. Female. Diet: Meat and bread. Gave dog ether from 10 a. m. to 11.30 a. m. Amount, 150 cc. Urine drawn before beginning of anæsthesia was negative to Fehling's, and the polariscope. Urine drawn at the end of anæthesia turned the plane of polarized light 1° to right. A specimen of this urine greatly reduced Fehling's solution.

Some yeast was added to a specimen of this urine and allowed to ferment for 22 hours. At the end of this time, the urine was filtered and examined by the polariscope. The plane of polarized light was not turned at all. The urine was also negative for Fehling's. This demonstrates clearly that the reducing property acquired by the urine is due to dextrose.

EXPERIMENT. No. 4.—Dog, No. 80. Female. Diet: Meat and bread. Dog was given ether from 9.05 to 10.05 a. m. Amount, 13.5 cc. Urine drawn before beginning of anæsthesia was negative for Fehling's. Catheterized at 3 p. m. and 105 cc. of urine obtained. Tested quantitatively by Benedict's method, it showed 0.7304 gm. dextrose.

These experiments will suffice to confirm the previous findings in the literature that ether causes a definite glycosuria which may make its appearance as early as 20 minutes after beginning the anæsthesia, and disappears by the end of 24 hours. The reducing property of the urine is due to dextrose.

To explain the occurrence of ether glycosuria, it is obviously first necessary to know what changes the anæsthetic has upon the sugar content of the blood. Previous experiments from the literature indicate that a hyperglycæmia precedes (6) and causes the appearance of sugar in the urine. The results are, however, not in great harmony, and an accurate study of the conditions in the blood seemed desirable at this point. Accordingly several experiments were made to ascertain whether a hyperglycæmia occurred after ether anæsthesia and how large an increase in sugar in the blood resulted.

Method.—Healthy adult female dogs were chosen for these experiments. They were all fed upon the same diet, namely, 200 gm. of lean meat daily, and as much water as they chose to drink. Each experiment was conducted in the following manner: Under aseptic conditions and local anæsthesia 50 cc. of blood was drawn from the jugular vein into a weighed Erlenmeyer flask containing 5 cc. of 1 per cent sodium oxylate. The whole was then weighed and the weight of the blood thus obtained. The animal was then anæsthetized with ether for two hours and at the end 50 cc. more of blood drawn from the same vein under the same procedure. The animal was then placed in a cage and the urine collected for 24 hours in a receptacle containing 5 cc. of toluol. The blood was examined for sugar by the excellent method of Oppler-Bertrand (7), and the urine for sugar by the method of Benedict and the polariscope.

A word must be said here regarding the influence of diet upon the occurrence of ether glycosuria. Seelig (9) reports that if animals are fed for a long time on carbohydrate diet they do not react to ether by showing a glycosuria. The time necessary for such feeding is generally 3-4 weeks for a medium-sized dog. Occasionally the condition can be brought about in 10 days. However, if fed on a meat diet, the animal responds to the administration of ether by a well-marked glycosuria. In all of our experiments, with the exception of the preliminary ones, the animals were fed upon the same diet, namely, 200 gm. of lean meat daily.

The results of the experiments are given below.

EXPERIMENT No. 5.—Female. Dog, No. B 18. Drew blood from right jugular vein before anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 112.30600
	Weight of flask + NaOx	= 54.86300
	Weight of blood	= 57.44300

Percentage of sugar = 0.059 per cent dextrose.

Etherized dog for 2 hours, using 250 cc. of ether and at end drew off blood as above.

		gm.
2.	Weight of flask + NaOx + blood	= 106.17210
	Weight of flask + NaOx	= 54.52900
	Weight of blood	= 51.64310

Percentage of sugar = 0.141 per cent dextrose.

Increase in sugar of blood due to ether anæsthesia = 0.082 per cent dextrose.

Remarks.—A marked increase in the percentage of sugar in blood.

EXPERIMENT No. 6.—Dog, No. B 15. Female. Drew blood from right jugular vein, before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 109.09420
	Weight of flask + NaOx	= 58.21425
	Weight of blood	= 50.77995

Percentage of sugar = 0.031 per cent dextrose.

Etherized dog for 2 hours, using 250 cc. of ether and at end drew off blood as above.

		gm.
2.	Weight of beaker + NaOx + blood	= 107.61190
	Weight of beaker + NaOx	= 58.29200
	Weight of blood	= 49.31990

Percentage of sugar = 0.215 per cent dextrose.

Increase in sugar of blood due to anæsthetic = 0.184 per cent. Urine was drawn by catheter at end of anæsthesia and 40 cc. obtained. This strongly reduced Fehling's solution.

EXPERIMENT No. 7.—Dog, No. B 15. Female. Blood taken from left jugular vein before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 115.22300
	Weight of flask + NaOx	= 62.49020
	Weight of blood	= 52.73280

Percentage of sugar = 0.058 per cent.

Etherized dog for 2 hours, using 250 cc. of ether, and at end drew off blood as above.

		gm.
2.	Weight of flask + NaOx + blood	= 110.96920
	Weight of flask + NaOx	= 58.13490
	Weight of blood	= 52.83430

Percentage of sugar = 0.113 per cent.

Increase in sugar in blood due to anæsthetic = 0.055 per cent.

EXPERIMENT No. 8.—Dog, No. B 63. Female. Blood taken from right jugular vein before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 83.47240
	Weight of flask + NaOx	= 31.34960
	Weight of blood	= 52.12280

Percentage of sugar = 0.041 per cent dextrose.

Etherized dog for 2 hours, using 250 cc. of ether, and then drew blood from vein as above.

		gm.
2.	Weight of flask + NaOx + blood	= 93.61430
	Weight of flask + NaOx	= 40.85850
	Weight of blood	= 52.75580

Percentage of sugar = 0.159 per cent.

Increase in sugar in blood due to anæsthetic = 0.118 per cent. The urine was collected for 24 hours. Amount, 230 cc., clear, no albumin. Sugar, 2.5596 gm.

EXPERIMENT No. 9.—Dog, No. B 65. Female. Blood taken from right jugular vein before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 87.82200
	Weight of flask + NaOx	= 35.63600
	Weight of blood	= 52.18600

Percentage of sugar = 0.055 per cent dextrose.

Etherized dog for 2 hours, using 250 cc. of ether, and then drew blood from vein as above.

		gm.
2.	Weight of flask + NaOx + blood	= 87.29390
	Weight of flask + NaOx	= 36.79590
	Weight of blood	= 50.49800

Percentage of sugar = 0.111 per cent dextrose.

Increase in sugar in blood, due to anæsthetic = 0.056 per cent. Urine collected for 24 hours. Amount, 480 cc., no albumin. Sugar, 1.0745 gm.

EXPERIMENT No. 10.—Dog, No. B 66. Female. Blood taken from right jugular vein, before beginning of experiment.

		gm.
1.	Weight of flask + NaOx + blood	= 88.22560
	Weight of flask + NaOx	= 38.36390
	Weight of blood	= 49.86170

Percentage of sugar in blood = 0.045 per cent dextrose.

Dog etherized for 2 hours, using 250 cc. of ether, and then blood drawn from vein as above.

		gm.
2.	Weight of flask + NaOx + blood	= 86.76400
	Weight of flask + NaOx	= 36.78050
	Weight of blood	= 49.98350

Percentage of sugar in blood = 0.094 per cent dextrose.

Increase in sugar in blood due to anæsthetic = 0.040 per cent dextrose. The urine showed a positive reduction to Fehling's test.

These experiments demonstrate conclusively that in healthy dogs following the administration of ether to the point of deep anæsthesia there occurs an increase of sugar in the blood, which then passes into the urine and causes the appearance of a reducing body in that fluid. In no case did sugar appear in the urine, unless the percentage of sugar in the blood was above normal.

These results are collected into tabular form for their more ready interpretation.

TABLE No. 1.

Dog.	Gender.	Diet.	Anæsthesia.	Length of anæsthesia.	Percentage of sugar in blood before anæsthesia.	Percentage of sugar in blood after anæsthesia.	Percentage of increase in sugar in blood.	Sugar in urine.
B 18	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.059%	0.141%	0.082%	+
15	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.031%	0.215%	0.184%	+
15	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.058%	0.113%	0.055%	+
B 63	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.041⅔	0.159%	0.118%	+ 2.560 gm. dextrose.
B 65	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.055%	0.111%	0.056%	+ 1.075 gm. dextrose.
B 66	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.045%	0.094%	0.049%	+

Seelig (9) was of the opinion that the extent of the glycosuria depended upon the amount of the anæsthetic used, i. e., that the longer the anæsthesia was continued the greater became the percentage of sugar in the urine.

Some experiments were conducted to test this point, and the results are given below:

EXPERIMENT No. 11.—Dog, No. B 61. Blood was taken from the right jugular vein before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 87.47120
	Weight of flask + NaOx	= 36.74400
	Weight of blood	= 50.72720

Percentage of sugar in blood = 0.034 per cent dextrose.

Dog etherized for 30 minutes, using 25 cc. of ether. Animal was just under the influence of the anæsthetic. Blood was taken at end of anæsthesia from right jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 93.215900
	Weight of flask + NaOx	= 39.448900
	Weight of blood	= 53.767000

Percentage of sugar in blood = 0.087 per cent dextrose.

The increase in sugar in the blood, due to the anæsthetic = 0.053 per cent dextrose. Urine, 150 cc. No reducing bodies.

The same experiment was repeated.

EXPERIMENT No. 12.—Dog, No. B 61. Female. Animal was bled from right jugular vein before beginning of anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 119.27020
	Weight of flask + NaOx	= 70.05150
	Weight of blood	= 49.21870

Percentage of sugar in blood = 0.046 per cent dextrose.

Dog was then etherized for 30 minutes with 25 cc. of ether. At end of anæsthesia, animal was bled from right jugular vein as above.

		gm.
2.	Weight of flask + NaOx + blood	= 111.08180
	Weight of flask + NaOx	= 60.47790
	Weight of blood	= 50.60390

Percentage of sugar in blood = 0.076 per cent dextrose.

Increase in sugar in blood, due to anæsthetic = 0.030 per cent. Urine collected for 24 hours. Amount 280 cc. Acid, albumin none, sugar none.

A second experiment was performed on the same dog, using 100 cc. of ether.

EXPERIMENT No. 13.—Blood taken before anæsthesia from right jugular vein.

		gm.
1.	Weight of flask + NaOx + blood	= 90.20300
	Weight of flask + NaOx	= 41.23510
	Weight of blood	= 48.96790

Percentage of sugar in blood = 0.043 per cent dextrose.

Dog etherized for ½ hour, using 100 cc. of ether. Dog was deeply under. Blood taken at end of anæsthesia from right jugular vein as above.

		gm.
2.	Weight of flask + NaOx + blood	= 85.19860
	Weight of flask + NaOx	= 39.77230
	Weight of blood	= 45.42630

Percentage of sugar in blood = 0.089 per cent.

Increase in sugar of blood, due to anæsthetic = 0.046 per cent dextrose. Urine collected for 24 hours, 610 cc. Albumin, 0; sugar, +. (Trace by Fehling's test.)

The results of all these experiments show that the extent of the hyperglycæmia is more or less dependent upon the amount of the anæsthetic used and the length of the anæsthesia.

TABLE No. 2.

Dog.	Gender.	Diet.	Anæsthesia.	Amount of ether used.	Time of anæsthesia.	Increase in sugar in blood.	Sugar in urine.
B 61	Female.	200 gm. of lean meat daily.	Ether.	25 cc.	30 min.	0.053%	Negative.
B 61	Female.	200 gm. of lean meat daily.	Ether.	25 cc.	30 min.	0.030%	Negative.
B 61	Female.	200 gm. of lean meat daily.	Ether.	100 cc.	30 min.	0.043%	+
B 15	Female.	200 gm. of lean meat daily.	Ether.	250 cc.	2 hrs.	0.184%	+
B 63	Female.	200 gm. of lean meat daily.	Ether.	250 cc.	2 hrs.	0.118%	+

The occurrence of a hyperglycæmia naturally suggests that we turn our attention to the liver as the most probable organ for its source. What effect does ether have upon the glycogen content of this organ? Seelig (10) reports that the percentage of glycogen in the liver is diminished after etherization. Another method of investigating the question appealed to us: What would be the effect of removal of the liver from the circulation, upon the occurrence of ether glycosuria? This condition could be brought about by establishing an Eck fistula; then, after the animal had recovered from the effects of the operation, the study could be carried out in the same manner as outlined in the previous experiment. The results should indicate conclusively to what extent the liver entered into the mechanism of ether glycosuria.

The experiments are given below. All the animals were upon the same diet, namely, 200 gm. of lean meat daily.

EXPERIMENT No. 14.—Dog, No. B 36. Female. An Eck fistula was made for us by Drs. Bernheim and Stone. The animal made an excellent, immediate recovery and was allowed to recuperate for one week. During this period, the dog was given a liberal amount of bones and water with the regulation 200 gm. of meat. Then she was operated upon aseptically and 50 cc. of blood withdrawn from the right jugular vein before beginning of the anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 94.24300
	Weight of flask + NaOx	= 44.40810
	Weight of blood	= 49.83490

Percentage of sugar in blood = 0.055 per cent dextrose.

Dog was then etherized for 2 hours, using 250 cc. of ether, and then blood was taken from right jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 121.50790
	Weight of flask + NaOx	= 66.85840
	Weight of blood	= 54.64950

Percentage of sugar in blood = 0.0779 per cent dextrose.

Increase in sugar in blood = 0.022 per cent dextrose, due to anæsthetic. No sugar in the urine.

Remarks.—The increase is very much less than when the liver is in the circulation.

EXPERIMENT No. 15.—Same dog was used again after a week's rest. No. B 36. Female. Blood taken from right jugular vein before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 108.91390
	Weight of flask + NaOx	= 61.19210
	Weight of blood	= 47.72180

Percentage of sugar in blood = 0.064 per cent dextrose.

Animal was etherized for 2 hours, using 250 cc. of ether, and then bled from right jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 120.32900
	Weight of flask + NaOx	= 66.89800
	Weight of blood	= 53.43100

Percentage of sugar in blood = 0.089 per cent dextrose.

Increase in sugar in blood due to anæsthetic = 0.025 per cent dextrose. No sugar in the urine.

Remarks.—Here again the increase in sugar in blood after anæsthesia is strikingly less than when the liver is in the general circulation.

The dog was turned over to Dr. Whipple for further experiments, at the conclusion of which the animal was killed and a splendid Eck fistula was found to have exsited.

A third experiment was conducted to further confirm these results.

EXPERIMENT No. 17.—Dog, No. B 48. Female. Weight 25 pounds. An Eck fistula was established upon this animal by Drs. Bernheim and Stone. The animal recovered well, and was treated post-operatively exactly as in the previous experiment. Blood was taken from right jugular vein before beginning of anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 89.62300
	Weight of flask + NaOx	= 39.43460
	Weight of blood	= 50.18840

Percentage of sugar in blood = 0.066 per cent dextrose.

Dog was then etherized for 2 hours, using 250 cc. of ether, and then bled from the right jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 86.95500
	Weight of flask + NaOx	= 39.97320
	Weight of blood	= 46.98180

Percentage of sugar in blood = 0.093 per cent dextrose.

Increase in sugar in blood, due to anæsthetic = 0.027 per cent dextrose. No sugar in the urine.

A fourth experiment confirmed the preceding ones.

EXPERIMENT No. 18.—Dog, No. B 48. Female. Dog bled from left jugular vein, before beginning of anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 95.68100
	Weight of flask + NaOx	= 46.64100
	Weight of blood	= 49.04000

Percentage of sugar in blood = 0.059 per cent dextrose.

Dog given ether for 2 hours, using 250 cc., and then bled from left jugular vein at end of anæsthesia.

		gm.
2.	Weight of flask + NaOx + blood	= 72.07830
	Weight of flask + NaOx	= 39.42550
	Weight of blood	= 32.65280

Percentage of sugar in blood = 0.050 per cent dextrose.

Remarks.—Here there is no increase in sugar in blood after ether, but a slight decrease *i. e.* 0.009 per cent dextrose.

These experiments suffice to show what part the liver takes in the mechanism of ether glycosuria. When the liver is removed from the circulation and consequently from the effect of the anæsthetic, there occurs practically no change in the percentage of sugar in the blood. This, taken in conjunction with Seelig's findings of a diminished glycogen content of the liver following ether anæsthesia, establishes the liver as the organ furnishing the increased sugar to the blood. Of course some circulation reaches the liver through the hepatic arteries, and this may account for the very slight change in the percentage of the blood-sugar, but other experiments in which the hepatic artery was tied and cut indicate that the influence of the hepatic artery is very slight.

A table of the results of these experiments is given below.

TABLE No. 3.

ECK FISTULA DOGS.

Dog.	Gender.	Diet.	Anæsthesia.	Length of anæsthesia.	Percentage of sugar in blood before anæsthesia.	Percentage of sugar in blood after anæsthesia.	Percentage of increase in sugar in blood.	Sugar in urine.
B 36	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.055%	0.077%	0.022%	–
B 34	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.064%	0.089%	0.025%	–
B 48	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.066%	0.093%	0.027%	–
B 48	Female.	200 gm. of lean meat daily.	Ether (250 cc).	2 hrs.	0.059%	0.050%	0.009%	–

In regard to the causes which induce the liver, under the influence of ether, to raise the sugar content of the blood, the literature is in much disagreement.

Edie (10) thinks that in an allied condition of asphyxia glycosuria, the cause lies in the presence of an excess of carbon-dioxide in the blood and tissues and not a poverty of oxygen.

Macleod (11) states that in asphyxia glycosuria, if the splanchnic fibers to the liver are severed, no glycosuria results. He also has demonstrated the presence of glycogenetic fibers to the liver in the splanchnics.

Moore and Roof (12) suggest that anæsthetics possess the power of combining with tissue protein, and in this way limiting the activity of the bioplasm, and its power of combining with bodies for the purpose of metabolism.

Lepine and Bonlud (13) state that glycosuria in asphyxia is caused by lack of oxygen, which results in the production of leucomaines which interfere with glycolysis.

Edie (14) further suggests that the anæsthetic attracts the sugar containing substances in the tissues, setting free sugar.

Seelig (15) claims to be able to remove the effects of ether by intravenous infusions of oxygen.

Thus it is evident that the suggestions as to the cause of ether glycosuria can be largely grouped into three categories:

(1) Due to excess of carbon-dioxide.

(2) Due to poverty of oxygen.

(3) Action through the splanchnic.

In regard to the first suggestion, it was generally noted that the blood taken at the end of anæsthesia was quite red and did not suggest a high content of carbon-dioxide.

Further, Seelig did not notice any degree of asphyxia in his animals and does not give much consideration to this explanation.

As regards the administration of oxygen with the ether, we have not been able to prevent the occurrence of a glycosuria by such a procedure.

The control of many functions of glands by nerves is such a well-established process in the body that the possibility of ether acting through the mediation of the splanchnic nerve seemed worthy of study, especially in view of the results of the splendid experiments of Macleod (17), in which he demonstrated the presence of glycogenetic fibers in these nerves.

Accordingly, experiments were undertaken after the following schema:

(1) Dogs were anæsthetized as above, to determine their initial hyperglycæmia.

(2) Then they were operated upon, and the splanchnic fibers going to the liver cut, together with the hepatic artery. It was found that many of the fibers were so intimately associated with this artery that they could not be severed without also cutting the artery.

(3) After the animal had recovered, the effect of ether was again tried.

The results are given in the protocols below.

EXPERIMENT No. 19.—Dog, No. B 63. Female. Diet: 200 gm. lean meat daily. Dog bled from right jugular vein before starting anæsthetic.

		gm.
1.	Weight of flask + NaOx + blood	= 83.47240
	Weight of flask + NaOx	= 31.34960
	Weight of blood	= 52.12280

Percentage of sugar in blood = 0.041 per cent dextrose.

Dog was anæsthetized for 2 hours, using 250 cc. ether, and then bled from same vein.

		gm.
2.	Weight of flask + NaOx + blood	= 93.61430
	Weight of flask +	= 40.85850
	Weight of blood	= 52.75580

Percentage of sugar in blood = 0.159 per cent dextrose.

Increase in sugar of blood, due to anæsthetic = 0.118 per cent dextrose. The urine was positive to Fehling's test.

The dog was operated upon after a few days' rest, and the splanchnics cut, together with the hepatic artery as described

above. After a week's rest, the dog was then subjected to the ether experiment in same manner as before. Blood was drawn from the left jugular vein, before beginning the anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 89.47000
	Weight of flask + NaOx	= 38.61760
	Weight of blood	= 50.85240

Percentage of sugar in blood = 0.040 per cent dextrose.

Dog was then anæsthetized for 2 hours, using 250 cc. ether, and bled at end of anæsthesia from left jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 92.09410
	Weight of flask + NaOx	= 41.39570
	Weight of blood	= 50.69840

Percentage of sugar in blood = 0.144 per cent dextrose.

Increase in sugar in blood, due to anæsthetic = 0.104 per cent dextrose. Urine was positive for Fehling's test.

Remarks.—Cutting the splanchnics had practically no effect on the occurrence of ether glycosuria, as shown by the table.

	Per cent dextrose.
Increase in sugar in blood before cutting splanchnics	= 0.118
Increase in sugar in blood after cutting splanchnics	= 0.104

Another experiment was performed under the same conditions.

EXPERIMENT No. 20.—Dog, No. B 65. Female. Dog was on diet of 200 gm. of lean meat daily. Blood taken from right jugular vein before beginning of anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 87.82200
	Weight of flask + NaOx	= 35.63600
	Weight of blood	= 52.18600

Percentage of sugar in blood = 0.055 per cent dextrose.

Dog was then anæsthetized for 2 hours, using 250 cc. of ether, and bled from right jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 87.29390
	Weight of flask + NaOx	= 36.79590
	Weight of blood	= 50.49800

Percentage of sugar in blood = 0.111 per cent dextrose.

Increase in sugar in blood due to anæsthetic = 0.056 per cent dextrose. Urine showed 1.0745 per cent dextrose.

Animal was allowed to recover for a week and then operated upon and the splanchnics cut, together with the hepatic artery. After a few days' rest the animal was again subjected to the ether experiment as above. Blood was taken from the left jugular vein before beginning of anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 96.54570
	Weight of flask + NaOx	= 45.73080
	Weight of blood	= 50.81490

Percentage of sugar in blood = 0.037 per cent dextrose.

Dog was then anæsthetized for 2 hours, with 250 cc. of ether, and at end of anæsthesia blood was drawn off from left jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 104.39320
	Weight of flask + NaOx	= 53.28520
	Weight of flask	= 51.10800

Percentage of sugar in blood = 0.114 per cent dextrose.

Increase in sugar in blood due to anæsthetic = 0.077 per cent dextrose. Urine showed 2.175 gm. dextrose.

Remarks.—The cutting of the splanchnics had no appreciable influence upon the glycosuria caused by the ether.

	Per cent dextrose.
Increase in sugar in blood before cutting splanchnics	= 0.056
Increase in sugar in blood after cutting splanchnics	= 0.077

Another experiment was performed under the same conditions.

EXPERIMENT No. 21.—Dog, No. B 66. Female. Dog on diet of 200 gm. of lean meat daily. Dog bled from right jugular vein before beginning anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 88.22560
	Weight of flask + NaOx	= 38.36390
	Weight of blood	= 49.86170

Percentage of sugar in blood = 0.045 per cent dextrose.

Dog was then etherized for 2 hours, using 250 cc. of ether, and bled from the right jugular vein at end.

		gm.
2.	Weight of flask + NaOx + blood	= 86.76400
	Weight of flask + NaOx	= 36.78050
	Weight of blood	= 49.98350

Percentage of sugar in blood = 0.094 per cent dextrose.

Increase in sugar in blood due to anæsthetic = 0.049 per cent. Urine was positive to Fehling's test.

Dog was then allowed to recover for about a week and then operated upon as in previous experiments. After a week's recovery, the ether experiment was again repeated. Blood taken from right jugular vein, before beginning of anæsthesia.

		gm
1.	Weight of flask + NaOx + blood	= 90.04270
	Weight of flask + NaOx	= 36.11640
	Weight of flask	= 53.92630

Percentage of sugar in blood = 0.044 per cent dextrose.

Dog was then etherized for 2 hours, using 250 cc. of ether, and then bled at end, from left jugular vein.

		gm.
2.	Weight of flask + NaOx + blood	= 93.72710
	Weight of flask + NaOx	= 43.65580
	Weight of blood	= 50.07130

Percentage of sugar in blood = 0.166 per cent dextrose.

Increase in sugar in blood due to anæsthetic = 0.122 per cent dextrose. Urine was positive to Fehling's test.

Remarks.—Here, again, cutting the splanchnic nerves did not remove the effect of ether causing a hyperglycæmia and glycosuria.

A fourth experiment is given in which the animal was operated upon and the splanchnics cut without having first determined the extent of the hyperglycæmia with the splanchnics intact. It is given because it adds to the completeness of the series.

EXPERIMENT No. 22.—Dog, No. B 47. Female. Dog was on daily diet of 200 gm. of lean meat. Splanchnics to liver were cut as in previous experiment and after a few days' recovery the ether experiment was begun. Animal was bled from the right jugular vein before beginning of anæsthesia.

		gm.
1.	Weight of flask + NaOx + blood	= 94.13240
	Weight of flask + NaOx	= 42.09400
	Weight of blood	= 52.03840

Percentage of sugar in blood = 0.0302 per cent dextrose.

Dog was then anæsthetized for 2 hours, using 250 cc. of ether, and bled from the left jugular vein at end.

		gm.
2.	Weight of flask + NaOx + blood	= 86.14350
	Weight of flask + NaOx	= 35.23920
	Weight of blood	= 50.90430

Percentage of sugar in blood = 0.143 per cent dextrose.

Increase in sugar in blood = 0.0841 per cent dextrose.

Remarks.—This confirms the preceding experiments. The results are put in tabular form for their more ready interpretation.

TABLE No. 4.

SPLANCHNIC NERVE EXPERIMENTS.

Splanchnics to liver.	Dog.	Gender.	Diet.	Anæsthetic.	Percentage of sugar in blood before.	Percentage of sugar in blood after.	Increase in sugar in blood.	Appearance of sugar in urine.	Amount of sugar in urine.
Intact.	B 63	Female.	200 gm. of lean meat daily.	Ether.	0.041%	0.159%	0.118%	+	....
Cut.	B 63	Female.	200 gm. of lean meat daily.	Ether.	0.040%	0.144%	0.104%	+	...
Intact.	B 65	Female.	200 gm. of lean meat daily.	Ether.	0.055%	0.111%	0.056%	+	1.0745 gm. dextrose.
Cut.	B 65	Female.	200 gm. of lean meat daily.	Ether.	0.037%	0.114%	0.077%	+	2.175 gm. dextrose.
Intact.	B 66	Female.	200 gm. of lean meat daily.	Ether.	0.045%	0.094%	0.049%	+	....
Cut.	B 66	Female.	200 gm. of lean meat daily.	Ether.	0.044%	0.166%	0.122%	+	....

These experiments show clearly that the anæsthetic causes its glycosuric effect just as well after the splanchnics to the liver are cut. They further show that with the hepatic artery excluded from the circulation the anæsthetic works its full effect just as well through the portal circulation. This parallels very closely the observations of Whipple and Sperry (17), that chloroform acts just as well and causes the same lesions in the liver when the hepatic artery is excluded from the circulation by ligation.

These results would lead us to think that the anæsthetic acts directly upon the liver, and in some unknown way stimulates that organ to increase the sugar content of the blood. Since the glycosuric effect of ether practically disappears when the liver is excluded from the circulation, we must, it seems reasonable, conclude that the cause of the increased sugar content of the blood lies within this organ, and is not due to any effect upon the muscle or other organ glycogen, or upon the circulating sugar in the blood.

The effect can be brought about by the path of the blood stream, since eliminating the liver from the influence of its glycogenetic fibers does not prevent the occurence of both the hyperglycæmia and glycosuria.

Further investigation is necessary to ascertain whether ether affects the activity of the glycolytic ferments.

Conclusions.

(1) Following the administration of ether to the point of deep anæsthesia, there results, in healthy adult dogs, a well-marked glycosuria.

(2) The reducing body in the urine is dextrose.

(3) The cause of the glycosuria is a definite hyperglycæmia.

(4) The liver is the organ which furnishes the increase in sugar to the blood, as shown by the absence of the occurrence of a hyperglycæmia and glycosuria when the liver is removed from the circulation by an Eck fistula.

(5) Severance of all the splanchnic fibres of the cœliac plexus going to the liver did not remove the hyperglycæmia and glycosuria elicited by ether.

NOTE.—During the time of preparation of this article, Hawk has published two communications, dealing with the subject of post-anæsthetic glycosuria. In one (18) he concludes that this type of glycosuria is due primarily to the effect of ether in stimulating the transformation of glycogen into dextrose. The second (19) paper deals more largely with the rate of urine formation under ether anæsthesia. There occurs an inhibition of the urine-forming function during the time anæsthesia is induced, but such inhibition is quickly followed by a stimulated urine flow which is initialed as soon as the period of anæsthesia terminates. The inhibition of the urine formation was probably due to the effect of ether in constricting the arterioles of the kidney's blood supply.

LITERATURE.

1. Ruschhaupt: Archiv für Experimentelle Pathologie und Pharmakologie, 1900, XLIV, 127-141.
2. Seelig: Archiv für Experimentelle Pathologie und Pharmakologie, 1905, LII, 481-494.
3. Hawk: American Journal of Physiology, 1903-1904, X, 37.
4. Macleod: American Journal of Physiology, 1907, XIX, 388-407.
5. Underhill: Journal of Biological Chemistry, 1905-1906, I, 113-130.
6. Seelig: Archiv für Experimentelle Pathologie und Pharmakologie, 1905, LII, 481-494.
7. Oppler-Bertrand: Zeitschrift für physiologische Chemie, 1910, LXIV, 393.
8. Seelig: Archiv für Experimentelle Pathologie und Pharmakologie, 1906, LIV, 206-216.
9. Seelig: Archiv für Experimentelle Pathologie und Pharmakologie, 1905, LII, 481-494.
10. Edie: Biochemical Journal, 1906, I, 455-473.
11. Macleod: Journal of the American Medical Association, 1910, LV, 2133.
12. Mone and Roff: Proceedings of the Royal Society, 1904, LXXIII, 382.
13. Lepine and Bonlud: Comptes rendus de l'Académie des Sciences, 1902, CXXXIV, 582.
14. Edie: Biochemical Journal, 1906, I, 455-473.
15. Seelig: Archiv für Experimentelle Pathologie und Pharmakologie, 1905, LII, 481-494.
16. Macleod: American Journal of Physiology, 1903-1904, X, 37.
17. Whipple and Sperry: Johns Hopkins Hospital Bulletin, 1909, XX, 278.
18. Hawk: Archives of Internal Medicine, 1911, VIII, 39.
19. Do: Idem, 1911, VIII, 174.

THE EFFECT OF OCCLUSION OF THE VARIOUS HEPATIC VESSELS UPON THE LIVER.

By M. C. Winternitz, M. D.,

Associate in Pathology, The Johns Hopkins University.

Although the intrahepatic branches of the hepatic vessels are terminal, their capillary communications are so abundant that, as a rule, embolism or thrombosis of either of them causes no interference with the circulation of the liver. Despite this fact, various pathological changes, varying from simple congestion to true red and white infarcts, characterized by coagulative necrosis in the area supplied by the occluded vessel or vessels, are recognized and have been reproduced experimentally. These will be briefly discussed and a few original cases added.

Occlusion of the Portal Vein.

Occlusion of the portal vein, either thrombotic or embolic, is not rare. This is very evident from Lissauer's report.[1] Among 26,687 cases which came to autopsy at the University of Breslau from 1878-1907, Lissauer found 68 instances of complete or partial thrombotic occlusion of the portal vein or its branches. Most of these occurred as a secondary manifestation in a number of conditions. Portal thrombosis, however, may be primary and is then characterized by a symptom complex of circulatory ileus, as in the case of Lewis and Rosenau.[2] These authors collected 20 other cases from the literature.

As a rule such occlusion has no effect upon the liver parenchyma, since the hepatic artery supplies the blood by the anastomosis between the two systems. That is, while the branches of the portal vein alone supply the acini of the liver with blood and the hepatic artery supplies the interlobular tissue, still the capillaries arising from the hepatic artery empty into the interlobular branches of the portal vein. In this way the hepatic artery, through its anastomosis with the interlobular vein, is capable of compensating when the larger branches of the portal vein are occluded. As long as the small branches of the portal vein are not involved, so long will the hepatic artery be able to nourish the liver parenchyma.

Etiology.—Lissauer concluded, from his analysis of the literature, that slowing of the blood stream is not in itself sufficient to bring about portal thrombosis, that "marantic" thrombi must be exceptionally rare, and that one of the following conditions is essential:

Primary authoctonus atheroma.

Inflammation of the vein wall by extension.

Compression of the vein.

Purulent pylephlebitis.

Lewis and Rosenau, however, conclude from their clinical and experimental studies that bacterial infection plays a very important rôle in portal thrombosis. This is in agreement with the findings of other authors—Welch,[3] etc., in thrombosis elsewhere.

Obliteration of the Portal Vein Without Hepatic Changes.

This subject has been reviewed very recently by M. Versé.[4] He cites, as a typical example of fresh thrombosis of the portal vein, a case reported by Saxer in 1902, where thrombi occluded all of the portal radicals. Despite this, the liver was only somewhat small and anemic. The circulation had evidently been carried on by the hepatic artery. Versé then quotes a number of cases of old thromboses of the portal vein.

1. A case of Umber's where the vein was occluded by a thrombus judged to be from 20 to 30 years old. This thrombus was 1 cm. long and just at the hilus of the liver. The liver was relatively small, but otherwise normal. No definite collateral circulation to the liver was determined. The splenic vein also contained a thrombus and the spleen was enormously enlarged.

2. A case described by Heller where the thrombus occluding the portal vein had been extensively canalized. The patient had suffered for many years from a very much enlarged spleen which gradually decreased in size. He died of a ruptured verrucose vein of the stomach. The liver showed no marked changes.

3. A case reported by Risel showed the formation of numerous new veins besides canalization of the thrombus which extended into the hepatic branches. The spleen was much enlarged. Death was caused by a fresh clot in the superior mesenteric vein.

4. A case of Pick's where death followed rupture of a varix of the œsophagus. The portal vein was occluded, and Pick considered that the thrombosis had been secondary to a true hemangioma arising in the wall of the portal vein.[5] An extensive collateral circulation had been established also.

Versé then includes a case of his own where an organized thrombus occupied the splenic and the larger branches of the portal vein. A tremendous collateral circulation had established itself to carry off the portal blood. This was effected through the colic, gastric, œsophageal, omental and left renal, by its communication with the adrenal, veins. The liver received a large amount of portal blood through a mass of cavernous vessels of which the original canalized thrombus

[1] Lissauer: Virchow's Arch., 1908, CXCII, 278.

[2] Lewis and Rosenau: Arch. Int. Med., 1909, III, 233.

[3] Welch: Tr. Ass. Am. Phys., 1900, XV, 441.

[4] Versé: Beiträge z. path. Anat. u. z. allg. Path., 1910, XLVIII, 520.

[5] Versé discusses the nature of this hemangioma. He does not agree with Pick that this is a true blastoma, but considers it a formation secondary to the thrombosis—as in his case.

formed only a small part. This mass of collateral caverns involved the entire hepato-duodenal ligament.

Experimentally the portal vein has been ligated repeatedly in the production of Eck fistulæ. In several of these cases reported by Whipple[6] the liver, 10 to 11 weeks after ligation of the portal, showed the following picture: "In one dog the fistula between the portal vein and vena cava was quite small (4 x 6 mm.) and the ligature about the portal vein above the fistula was not effective, the opening admitting only the points of the scissors. In the other animal the fistula was quite large and the ligature of the portal vein was efficient.

"The livers were practically the same in both cases. The organ was small, flabby, and rather tough. The lobules were small, presenting a brown, translucent edge and minute central yellow dot. Microscopically there was considerable atrophy and fatty degeneration of the central half of the liver lobule."

In our autopsy reports the following cases of thrombosis of the portal vein without marked hepatic changes have occurred:[7]

1. O. W., white, age 49 years. Autopsy No. 175.

Anatomical Diagnosis.—Carcinoma of the stomach; metastases to the gastro-hepatic glands; *carcinomatous thrombus of the portal vein;* multiple carcinomata of the liver; ascites; hydrothorax (right); emphysema; bronchiectasis; bronchitis; bronchopneumonia with fresh pleurisy.

Liver is very large, covered by tumor masses. The hepatic artery is slightly thickened. The portal vein is of normal size. At its very entrance into the liver there projects into it a large, smooth carcinoma nodule (4 x 2½ cm.). The veins arising in the region of the thrombus are likewise filled with the tumor tissue, and a large mass in the left lobe of the liver is directly continuous with the vein thrombus.

There is in this case no note which would indicate any change in the hepatic tissue resulting from the portal occlusion.

2. A. B., white female, age 59 years. Autopsy No. 214.

Anatomical Diagnosis.—Syphilitic deformity of the liver of extreme degree; chronic passive congestion of spleen with perisplenitis and perihepatitis; chronic thickening of peritoneum, especially around the liver; *recent portal thrombosis;* fat necrosis (slight); acute diffuse peritonitis; chronic diffuse nephritis; mitral insufficiency; hypertrophy of left ventricle; calcification in the wall of splenic vein with parietal thrombus.

The portal vein is very wide, circumference 6½ cm. Just as it enters the liver its lumen is filled with a fresh grayish-red thrombus adherent in places to the intima, but in general easily removed. It extends a short distance into the main branches of the vein and looks very recent in its formation. The vessels in the hepato-duodenal ligament are enveloped in a mass of dense fibrous tissue.

Aside from a marked syphilitic cirrhosis, no lesion was found in the liver. Here again the portal occlusion was without effect. The etiological factor probably was syphilis.

[6] Whipple and Sperry: Johns Hopkins Hosp. Bull., 1909, XX. 278.

[7] The protocols will be abstracted as briefly as possible. Only those parts of particular interest to the subject at hand will be included.

3. F. R., white male, age 37 years. Autopsy No. 262.

Anatomical Diagnosis.—Tuberculous fibrous phthisis—both upper lobes; amyloid infiltration, spleen and kidneys; tuberculous ulceration of large and small intestine; *thrombosis of intrahepatic branches of portal vein.*

Liver.—1250 grams. Surface smooth. Margin round. Lobules visible. Consistency rather increased. Portal vein large, 2 cm. in diameter. Hardened sections of liver show slight increase in connective tissue. Thrombi in portal veins with extensive liver-cell emboli in same vessels. Slight dilatation of the capillaries.

4. L. G. Autopsy No. 462. Dr. Flexner.

Anatomical Diagnosis.—Diffuse suppurative cellulitis of left leg (streptococcus); ascites; chronic adhesive peritonitis; chronic perisplenitis; perihepatitis; *thrombosis of the portal vein;* chronic diffuse nephritis with acute exacerbation; chronic pleuritis, etc.

Liver.—1700 grams, 21 x 15 x 9 cm. It is everywhere adherent. The capsule is thickened, white fibrous-looking and in places reaches 4 mm. in thickness. On section it presents a mottled aspect. The surface is in general cloudy, deep reddish brown in color, with many lighter yellowish areas. Heavy bands of connective tissue proceed in from the porta and the capsule. By this means circumscribed areas of liver tissue are completely marked off. In general the lobules are more distinctly isolated than normally, and the central veins are quite prominent. The consistency of the liver is much increased. In the portal vein are thrombi. The main branch, beginning at the junction of the principal abdominal veins, is almost completely filled by a mixed thrombus which is only slightly adherent. At the entrance into the liver the vein is filled with a more firmly adherent, laminated, somewhat softened thrombus which does not fill the lumen. Some of the principal branches of the portal vein in the liver contain thrombus masses, some of which are recent, scarcely adherent and continuous with the laminated thrombus.

Microscopically there is an increase in connective tissue plus fatty degeneration of the liver cells.

It is quite probable that the mottled appearance of the liver in this case is related to the portal occlusion. The coarse bands of fibrous tissue also suggest a syphilitic cirrhosis.

5. B. S., white female, age 51 years. Autopsy No. 483.

Anatomical Diagnosis.—Carcinoma of the head of the pancreas with extension into the duodenum and stomach; multiple metastases to lymph glands, both adrenals, liver and lung; *thrombosis of portal vein.*

The portal vein is thrombosed just before it enters the liver by a partially decolorized thrombus mass. Aside from the tumor metastases, section of the liver is brownish red in color and homogeneous.

6. L. F., white male, age 45 years. Autopsy No. 567.

Anatomical Diagnosis.—Perforating ulcer of stomach; old adhesive peritonitis around perforation; ulceration into splenic artery and into small pyloric artery; thrombosis of splenic artery; extension of clot into cœliac axis and abdominal aorta; infarction of spleen; *complete thrombosis of splenic vein, with extension of thrombus into portal vein;* thrombosis of many interlobular veins in liver, etc.

Liver is rather small (22½ x 16 x 5 cm.). Surface smooth. Left lobe is adherent to the stomach. On section organ is soft and flabby, but tough. In the right lobe the lobulation is marked. The general color is brownish red. The left lobe is homogeneous in color. The lobules are scarcely visible. In a number, but not in all, of the interlobular veins of the right lobe, there are antemortem clots, reddish and sometimes with white centers. These are continuous with a small thrombus in the portal vein. There are very few thrombi in the interlobular veins

of the left lobe, although they occur, and a small thrombus enters the large portal radical of the left lobe.

Here the thrombus occluding the portal vein had no effect upon the liver parenchyma. No doubt the localized peritonitis was the direct cause of the thrombosis.

7. H. S., white male, age 49 years. Autopsy No. 649.

Anatomical Diagnosis.—Diabetes mellitus; cirrhosis of liver; *thrombosis of portal*, splenic and mesenteric veins; hemorrhagic infarction of intestine; acute peritonitis (serofibrinous, due to gas bacillus); subcutaneous œdema and emphysema, etc.

Liver is firmly bound to the diaphragm over the right lobe. Here the capsule is much thickened (4 mm.) and of cartilaginous appearance. Surface of liver is rough and coarsely granular. On section coarse cirrhosis is visible. The cut surface has a yellow color. Portal vein contains a decolorized thrombus firmly adherent to the wall of the vein, and extending beyond the hilum into some of the main branches.

No definite cause for the thrombus formation in the liver was evident in this case. It is probable that portal stasis referable to the cirrhosis was an important factor.

8. C. H. C., white male, age 58 years. Autopsy No. 850. Dr. Flexner.

Anatomical Diagnosis.—Thrombosis of mesenteric veins; necrosis and gangrene of small intestine; general fibrino-purulent peritonitis; abscess in omentum (operation wound); extension of venous thrombus into portal vein; congestion of liver and spleen.

Liver free from adhesions, weight 2500 grams. On section cloudy, markings distinct owing to moderate congestion. Consistency not increased.

Mesenteric vein is thrombosed. The thrombus in the main branch is partly decolorized, dry and adherent to the vein wall, etc. The thrombus can be traced into the portal and extends into the hilum of the liver. The main branch of the portal vein is apparently completely occluded by the firm, grayish-red mass which is moderately adherent to the vein wall. Beyond the main vein and extending into the left branch, but not into the right, is a recent soft red clot.

Here the occluding mass was a propagative thrombus from the mesenteric vein.

9. Outside Case. Autopsy No. 1398. Dr. MacCallum.

Anatomical Diagnosis.—Primary splenomegaly; *thrombosis of splenic mesenteric and portal veins;* splenic and intestinal infarcts; post mortem gas bacillus invasion.

The *liver* is bound to the diaphragm and surrounding viscera by fibrous adhesions. The portal veins on section are everywhere totally or partly occluded by thrombus masses which are fairly adherent to the vein wall. The liver tissue is much distintegrated by gas formation. The splenic vein is dilated to a diameter of 5 cm. and is distended with an elastic chicken-fat clot which shows points of opacity. This clot can be traced into the portal radicals. It completely occludes the portal vein throughout its length. As the clot approaches the liver it becomes darker. On section it is almost diffluent, especially in the more central part, where it has a purplish-brown color. On the lesser curvature and serous surface of the stomach there are several distended veins which are completely occluded by thrombi, as are also the omental veins.

Microscopically the clot in the mesenteric vein is organized and partly canalized. Surrounding the vein is a sheath of very vascular tissue.

The liver shows microscopically no definite increase in connective tissue. The spleen has a thickened capsule, but the trabeculæ are not much thickened and the connective tissue of the sinuses is much increased.

10. F. S., white male, age 62 years. Autopsy No. 1464. Dr. Marshall.

Anatomical Diagnosis.—Carcinoma of stomach with metastases to liver, etc.; *occlusion of portal vein at hilum of liver by metastases; propagated thrombus in hepatic branches of portal vein, etc.*

Liver weighs 1300 grams, measures 26 x 15 x 6½ cm. Consistency decreased. Surface uneven, due to tumor nodules, etc. On section liver substance is pale, rather opaque and fatty. A tumor nodule is found completely blocking the splenic vein, about 7 cm. from junction of splenic and portal veins. The metastasis extends into the portal, completely occluding it beyond the hilum of the liver. It is firmly attached to the vessel wall, giving it a diameter of 1 to 3 cm. Where this growth ends beyond the hilum of the liver a thrombus begins, extending into the main branches of the portal vein.

11. J. M., white male, age 48 years. Autopsy No. 2706. Dr. Whipple.

Clinical Diagnosis.—Primitive splenomegaly.

Anatomical Diagnosis.—Chronic splenic tumor; sclerosis of splenic and portal veins; cirrhosis of liver and *thrombosis of portal branches;* chronic passive congestion of pancreas and intestine; œsophageal varices with rupture; hemorrhage into the stomach and intestine; anemia; chronic fibroid pulmonary tuberculosis; chronic tuberculous lymphadenitis; miliary tubercles in spleen and liver.

Spleen weighs 1050 grams; measures 21 x 14 x 6½ cm. Splenic vein shows definite sclerosis everywhere, especially marked after one leaves the hilum of the spleen. At the junction of the splenic vein with the mesenteric vein a large thrombus mass is seen tightly adherent to the anterior wall of the mesenteric veins, but only partly occluding its lumen. Thrombus is of a gray color showing definite ridges and furrows on its surface. The portal vein, however, is completely occluded by a firm thrombus mass which shows some fresh central blood clot, but is mostly made up of gray translucent tissue. As one goes upward, one finds the two branches of the portal vein completely obliterated by similarly appearing thrombus masses. These thrombi show fibrous translucent tissue at the margin, merging into the vessel wall, while the central portions show a greater or lesser degree of brownish-red blood clot, or even fluid blood. Some of these vessels seem to show small channels full of fluid blood, in the organized fibrous thrombus mass.

Liver weighs 1200 grams; measures 22 x 16 x 7 cm. Its upper surface, as a rule, is pretty smooth and of a pale brown color. Near its anterior margins it shows considerable granulation of its surface, prominent nodules of opaque tissue alternating with depressed areas in which are dilated blood vessels. The lower surface of the liver has a more marked granular appearance, especially around the fissure at the entrance of the portal structures. Cut surface in the upper portion shows great anemia, but little increase in connective tissue. As one approaches the transverse fissure, however, the connective tissue becomes considerable in amount; embedded in it are irregular nodules of opaque yellow appearance, apparently hypertrophied islands of liver tissue. This connective tissue increase seems localized pretty sharply around the branches of the portal vein and becomes progressively greater in amount as we approach the larger thrombosed branches of the portal vein.

The *œsophagus*, opened up from behind, shows tremendous distention of the veins underneath its mucosa. These veins are very tortuous; some of them, dilated to a diameter of 3 mm., form little miliary saccular aneurysms which bulge very definitely from the walls of the dilated venules. Some show superficial necrosis of the mucosa covering them and are seemingly just on the point of

rupturing. Twelve cm. above the cardiac junction is a small erosion 3 x 1 mm. with clean edges, communicating directly with the lumen of the large dilated veins, into which a good-sized probe can be passed with ease. Blood can be squeezed through this opening. The stomach contains 650 cc. of dark jelly-like blood clot. Its mucosa is intact everywhere. Just around the cardiac orifice it shows a network of large tortuous dilated veins, which, however, only persist for a distance of 5 cm. from the junction with the œsophagus. The duodenum is normal. Dissection of the dilated veins around the cardiac orifice shows them to communicate with branches of the splenic vein given off 3 or 4 cm. from the origin of the vein at the hilum of the spleen. A few of the smaller veins in this position seem to anastomose with the veins along the lesser curvature of the stomach.

The *liver* shows an increase in connective tissue between the lobules. This, however, is not uniform, being most marked in sections taken from the region of the transverse fissure. The connective tissue is sharply confined to the margins of the lobules and does not extend into the central portion, except where the lobule has undergone complete degeneration. The portal vein shows a thrombus made up of old fibrous tissue into which numerous capillaries have grown. Some of these have become enlarged to a considerable size and contain fresh blood. The bile ducts in this neighborhood show signs of active proliferation.*

The above report of Autopsy No. 2706 has been given in greater detail because the findings do not correspond with the clinical diagnosis of primitive splenomegaly.

These 11 cases do not present any new features. In all, the portal vein and its radicals alone were involved. In all, the finest interlobular veins were free. In all, the general circulation was maintained to a sufficient extent to prevent any striking changes in the liver directly attributable to the occlusion. In 3, the thrombi were the direct result of tumor invasion; in 2, they were the result of a localized peritonitis (one of these was possibly a syphilitic process); in 1, they accompanied a syphilitic liver; in 2, they were secondary to cirrhosis; in 1, they were a direct extension from a thrombosed mesenteric vein; in 1, a secondary process occurring in the course of a general tuberculosis, where there was amyloidosis; and in 1, the process seemed primary.

It is interesting to compare the findings in the above cases with the much more extensive series of Lissauer. In his series, 6 of the 68 cases of thrombosis of the portal vein were associated with atrophic cirrhosis of the liver; in 7, with syphilis of the liver; in 2, with primary carcinoma of the liver; in 7, with carcinoma of the stomach, accompanied by metastatic growths in the liver; in 2, with secondary carcinoma of the liver; in 6, with primary carcinoma of the biliary passages; in 9, with gall-stones and inflammatory lesions of the gall-bladder; in 10, with diseases of the pancreas; in 1, with suppurative inflammation of the umbilical vein; in 6, with diseases of the spleen; in 6, with gangrenous appendicitis; in 2, with carcinoma of the intestine; in 1, with a pelvic abscess; and in 1, with no definite cause.*

Two cases, Nos. 9 and 11 of our series, deserve a word of comment. Versé points out that the tremendous enlargement of the spleen, the anemia which so often occurs, and the integrity of the liver may often suggest the clinical picture of Banti's disease. Very great enlargement of the spleen may result from simple vascular changes accompanying portal thrombosis; and he concludes that only then may we speak of a primary splenomegaly, when absolutely every other organic cause has been excluded. The above cases are not instances of primary splenomegaly, since the extensive thrombosis is quite enough to explain the findings.

It is essential to remember portal thrombosis in the differential diagnosis of splenomegaly.

Embolic or Thrombotic Areas of Congestion.

Despite the extensive anastomosis between the branches of the portal vein and the hepatic artery, in rare instances and under accessory circumstances a condition somewhat resembling the macroscopic picture of hemorrhagic infarction, and often spoken of as the "atrophic red infarct of Zahn," may follow plugging of branches of the portal vein. The "atrophic red infarcts of Zahn" are triangular, rectangular or irregularly wedge-shaped areas with their apices at the occluded vessel. As a rule they are dark red or reddish-brown, but pale areas have also been observed. Microscopically there is simply a congestion of the intralobular capillaries with slight atrophy of the liver cells and possibly some pigmentation. It is of importance to note that necrosis does not occur in these areas. Ruczynski[9] explains their production in the following way. The blood from the portal vein no longer flows into the hepatic vein and the latter is only poorly filled by the blood of the hepatic artery. As a result there is a stasis in the hepatic vein due to the deficient *vis a tergo*, and the picture of a congested liver with dilatation of the central veins and capillaries and atrophy of the liver columns is gradually produced. This is the condition which was described by Zahn.[10] Orth[11] had described it previously and in his text-book expresses clearly that they are the result of an aseptic embolic or thrombotic process. He calls them areas of circumscribed congestion, atrophy or cyanotic atrophy which may be viewed as a type of hemorrhagic infarction but never as a complete infarct.

Many observers have described this picture. Bertog[12] described two cases in which a "chronic red atrophy" of the liver was the result of decreased portal blood supply from compression of portal roots by chronic peritonitis. He considered that any hindrance to the free flow of portal blood to the liver might produce an atrophy of the liver similar to what occurs in a liver of congestion. Cohnheim and Litten[13] described a "nutmeg" liver involving the part of the gland

* There are two other cases of portal thrombosis in our first 3500 autopsies: one autopsy, No. 224, where there was only a small parietal thrombus of the portal vein, and autopsy No. 1409, where the picture in the liver was so obscured by complicating conditions that the result of the portal occlusion upon the hepatic parenchyma was indefinite.

* Quoted by Lewis and Rosenau.

[9] Ruczynski: Ztschr. f. Heilk., 1905, XXVI, 147.

[10] Zahn: Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte 1897. Leipz. 1898, Part 2, p. 9; or Centralbl. f. allg. Path., 1897, VIII, p. 860.

[11] Orth: Lehrbuch der Path. Anatomie, 1887, I, 917.

[12] Bertog: Greifswalder Beiträge, 1863. Quoted by Chiari.

[13] Cohnheim and Litten: Virchow's Archiv., 1876, LXVII, 153.

supplied by an occluded portal radical. Klebs [14] cited the presence of wedge-shaped areas after occlusion of radicals of the portal vein; these areas showed microscopically only a granular degeneration. Wagner [15] described an instance of narrowing and thrombosis of several portal radicals resulting in deep red or pale wedge-shaped areas. Köhler [16] reported three cases of cyanotic atrophy after occlusion of large portal radicals. His first case concerned a man who, 7 days before death, underwent an operation, *i. e.*, excision of rectum for carcinoma. At autopsy one of the portal veins contained an antemortem clot and the liver supplied by the branch showed the usual picture macroscopically. Sections showed less fat in the atrophied cells and an increase of brown pigment. The second case was one of malignant tumor of the peritoneum with thrombosis of a portal radical and the usual picture of pseudo infarction. In the third case there was a septic embolus in the right branch of the portal vein, and a large hyperemic wedge-shaped area of liver containing multiple small abscesses corresponded to the distribution of the occluded vein. The thrombus arose in the splenic vein. Köhler concluded that not only portal thrombosis, but also weakened heart action was essential to obtain the above picture of congestion. He considered the atrophy of the liver cells to result from pressure of the dilated capillaries and inactivity of the liver cells. Pitt [17] added three more cases. The first concerned an individual who died 5 days after an operation for relief of an incarcerated scrotal hernia. The liver showed an atrophic zone 2 inches in diameter and the corresponding vein was occluded. Sections only showed dilatation of the capillaries. His second case, an old man who died of cerebral hemorrhage, showed corresponding to many thrombosed branches of the portal vein, numerous sharply demarcated pale or dark areas with dilatation of the capillaries in the latter. In the third case there was a pale area of liver, the result of embolic plugging of a portal branch following operation for ovariotomy. Ruczynski [18] explained the pale areas of the third and second cases by the persistence of anemia following the portal occlusion. Chiari [19] in a very comprehensive report published in 1898 collected most of the above cases and added 17 cases observed by him from 1877 to 1898. On account of the large number of personal observations he is inclined to consider this condition not at all uncommon. Of his 17 cases, 15 resulted from emboli arising in branches of the portal vein. These he subdivided into those cases where the thrombosis of the portal roots followed by hepatic emboli occurred without any external influence (7 cases) and those where some operative procedure involving the portal roots occurred shortly before death—(8 cases). The two remaining cases resulted from thrombi arising within the intra-hepatic radicals of the portal vein.

Of the group of emboli occurring without external cause, 4 were carcinomatous in nature, 1 occurred in a case of "marasmus," 1 in typhoid ulcerative enteritis and 1 originated from a thrombus formed in the splenic vein, the result of pressure from an aneurysm of the splenic artery. In several cases of the second group the thrombi in the roots of the portal vein were the direct result of ligatures applied to these branches at the time of operation.

Chiari considered the dark areas of the liver to be a purely mechanical result following occlusion of the large branches of the portal vein, namely, local areas of congestion involving primarily the central vein and the neighboring capillaries of the central portion of the lobule with atrophy of the liver cells. The smallest branches of the portal vein in the affected areas of the liver were free of obstruction. Similarly the central veins and the hepatic arteries in these areas were uninvolved. Blood extravasation only occurred twice and then only in small amounts. Necrosis of the liver cells was never found. Chiari's findings confirmed the observations of other authors concerning the origin of these areas, *i. e.*, that they were only circumscribed areas of congestion. The liver cells received enough fresh blood through the inner portal roots to exist. The *vis a tergo*, however, was not sufficient to keep up the normal circulation, and as a result there was a reflux congestion of the blood from the right auricle which, together with the constantly decreasing nourishment of the liver cells, caused them to atrophy. It was worthy of note that in a number of cases the liver cells of the affected zone, were practically fat free, while in the remaining liver the fat was present in considerable amounts. This Chiari explained by the stoppage of the flow of the portal blood through the area. Finally Chiari concluded with Köhler that simple occlusion of branches of the portal vein was not sufficient to bring about the formation of the so-called atrophic red infarct. There must be added to the occlusion one of the following conditions:

a. Weakening of the arterial current to the liver.
b. Venous congestion.
c. A combination of the two above conditions, or
d. Impaired cardiac action.

This latter he considered to be the most important.

Ruczynski adds several more cases.

That of Lazarus Barlow, concerned a young man, who had been crushed between the buffers of two railroad cars. Death followed in three days. At autopsy there was a large tear in the right lobe of the liver. In the center of this tear was a thrombosed portal vein and corresponding to the distribution of this vessel was a large wedge or grayish-white tissue. Lazarus Barlow considered this an anemic infarct, but Ruczynski disagreed with this diagnosis since the author does not mention in his microscopical findings the presence of necrotic liver cells.

Longcope reports a case where, besides numerous metastatic cancer nodules from a primary gastric growth, there was a deep red triangular area whose base measured 3 cm. The portal vein leading to this discolored zone was occluded.

Finally, Versé [20] reports a case where in a young woman

[14] Klebs: Handbuch der Path. Anatomie, 1896, I.
[15] Wagner: Arch. f. klin. Med., 1884, XXXIV, 520.
[16] Köhler: Arb. a. d. path. Institut in Göttingen, 1893, 121.
[17] Pitt: Tr. Path. Soc. Lond., 1895, XLVI, 74.
[18] Ruczynski: *Loc. cit.*
[19] Chiari: Ztschr. f. Heilk. 1898, XIX, 475.
[20] Versé: Verhandl. d. deutsch. path. Gesellsch., 1909, XIII, 314.

with periarteritis nodosa, large, circumscribed, depressed areas of congestion followed occlusion of small portal veins.

Zahn[21] studied the effect of injection of sterile mercury into the mesenteric veins of dogs. After eight days, the shortest period, there were red, triangular areas in the liver which were typical of the atrophic red infarct in 35 days. They showed microscopically the picture of congestion and atrophy of the hepatic parenchyma, but there was no necrosis.

The following three cases belong to this group of liver changes following occlusion of the portal vein radicals.

The first case is so unique that a rather detailed account will be given.

W. K., white male, age 40 years. Admitted to the medical clinic of the Johns Hopkins Hospital, January 5, 1911, complaining of stomach trouble. Previous to present illness, history was negative. P. I. began 5 months before admission, with sudden, acute abdominal pain and vomiting. This was first blackish and gradually became paler. The vomiting persisted and there was loss of weight, amounting to 100 pounds. Examination revealed nothing of importance except a HCl deficit of 10, and a total acidity of 8; and an increased resistance in left epigastrium. The Wassermann reaction was negative. Occult blood was repeatedly demonstrated in the stools. On March 20, an exploratory laparotomy was performed by Dr. Finney. The stomach was found greatly dilated. Its walls were atonic, but there was no evidence of new growth.

The duodenum was greatly enlarged and relaxed, being almost twice its normal diameter, with soft, flabby walls. Aside from some dense adhesions, some of which were severed, nothing of importance was observed. The patient did not recover from the operation.

Died, 8 p. m., March 21, 1911.

Autopsy, 10 p. m., March 21, 1911. Autopsy No. 3519. Dr. Winternitz.

Anatomical Diagnosis.—Chronic inflammatory stricture of the jejunum, probably following strangulation of the bowel after a volvulus; multiple thrombi in the mesenteric vessels; dilatation of stomach and duodenum; extensive scarring and atrophy of wall of jejunum; chronic adhesive peritonitis, particularly marked about the region of the stricture; chronic mesenteric lymphadenitis; pressure of inflammatory mass on retroperitoneal tissues, resulting in thrombosis of left renal vein; slight atrophy of left kidney; (exploratory laparotomy); dislodgment of portion of thrombus in renal vein; embolus into one of the smaller radicals of the pulmonary artery with hemorrhagic infarction of lung. *Dislodgement of mesenteric thrombus; embolism into large right portal vein with formation of a localized area of congestion in the liver.*

Abdominal cavity. The adhesions are chiefly in the left hypochondrium. The omentum is bound tightly to the pancreas and this with the duodenum and spleen forms one compact mass, over which the jejunum passes emerging from a small knot of adhesion.

Liver measures 28 x 20 x 9½ cm. Its surface is smooth. On section it presents an extremely striking picture. A large area in the right lobe has a much deeper brown color than the remaining liver tissue. This area is irregularly wedge-shaped extending to the hilus of the gland where the apex of the triangle is found. Throughout this darker portion of the liver the portal vein radicals are occluded by large ante mortem clots which are quite friable. These converge to one large hilic branch of the portal vein where a large non-adherent clot is found. The two areas of liver, namely, the darker area in which the portal vessels are occluded and the surrounding paler brown areas present otherwise only minor differences. In both zones the lobules are distinct. In the darker portion they are somewhat smaller.

[21] Zahn: *Loc. cit.*

Microscopically, in the area involved by the occluded portal radical, the liver cells stain paler; the columns are somewhat thinner, the vessels slightly dilated. The change is so slight that it might not be noted were one's attention not specially directed towards it. Neither the interlobular veins, hepatic arteries nor the central veins are involved by thrombus.

This case represents a typical example of the result of embolism of a large portal radical. The embolus arose from a thrombus in the mesenteric vein which was probably dislodged at the time of operation. The area of pseudo infarction in the liver is consequently very young, probably less than 24 hours.

13. R. F., white male, age 40 years. Autopsy No. 1691. Dr. Opie.

Anatomical Diagnosis.—Cholelithiasis; calculus impacted in diverticulum of Vater only partly filling it and occluding its duodenal orifice; acute hemorrhagic pancreatitis; disseminated abdominal fat necrosis; partial thrombosis of splenic vein; *embolism and thrombosis of portal vein.*

Liver weighs 1350 grams. Surface is smooth. Upon the upper surface of the right lobe are three irregular, very slightly depressed areas conspicuous from the fact that they are of a dull red color while the remainder of the surface is yellowish. The cut surface has a bright yellow color. The periphery of the lobules are golden yellow, the central part reddish, corresponding to the areas mentioned on the surface, on section; the tissue below has a similar appearance, the corresponding area being narrower as the surface becomes distant (*i. e.* irregularly wedge-shaped). Here this tissue is of a dull red color. Within such areas are seen sections of veins plugged, and distended with red thrombus. These are found to be portal veins. The vein in one of these areas has a diameter of about 4 mm. It is plugged with a red thrombus, which stops abruptly at the apex of the wedge, where it ends in a yellowish-white embolus. In addition to these large areas mentioned, several distinctly wedge-shaped smaller ones are present. The large portal branches are normal.

Microscopically. Within the lobules, usually at a distance from the portal spaces, are areas where the liver cells are clear and unstained with eosin in contrast to those about. With the high power the protoplasm is entirely unstained, but is slightly granular. The cell body is somewhat swollen. The nucleus is smaller, somewhat irregular, and no longer vesicular, staining homogeneously. In the center of one of these areas, a group of 10 to 12 cells whose protoplasm takes a conspicuous deep eosin stain is found. The nuclei are preserved; many polymorphonuclear leucocytes occur between these cells. (This case was reported by Opie in the JOHNS HOPKINS HOSPITAL BULLETIN, 1901, under the title, "The Etiology of Acute Hemorrhagic Pancreatitis").

14. B. V., 1908-9, D. W. Died, February 19, 1908, 2.15 p. m. Autopsy, February 20, 1908, 11.30 a. m. Dr. Meloy.

Anatomical Diagnosis.—Infected ovarian cyst; multiple miliary abscesses (operation); acute and chronic peritonitis; chronic diffuse nephritis (large white kidney); infarct of spleen, *zone of congestion of liver corresponding to distribution of occluded portal vein by thrombus;* amyloidosis; chronic perihepatitis and perisplenitis; anemia; emaciation; polypoid œdematous tumors of bladder.

Unfortunately no other data concerning this case was available. At the time of autopsy, however, the liver was practically identical in appearance with that of Case 12. Microscopically, too, there was no evident change in the organ. It is probable that here also there were thrombi in the portal roots which only reached the intrahepatic branch after operation.

To briefly summarize, obstruction of the large branches of the portal vein may cause irregular wedge-shaped areas of congestion, and in rare instances of anemia, in the liver. These are not true infarcts since they show microscopically only a dilatation of the central veins and intralobular capillaries, together with atrophy of the liver cells and no necrosis. Such an area may shrink considerably. This shrinkage is due to atrophy of the liver parenchyma, but to what extent pressure of the dilated capillaries, decreased nutrition, actual necrosis, or inactivity of the cells affects this atrophy is a problem inseparably associated with the still unsettled question of the atrophy of the liver occurring in chronic passive congestion due to general causes.

In all these cases the smallest branches of the portal vein in the congested zones were free of obstruction. The hepatic vein and artery were always unobstructed. The blood reached these zones through the inner portal vein radicals, but not in sufficient quantity to keep up the normal flow. This allowed a reflux from the larger hepatic vein which resulted in congestion. It must be repeated that occlusion of the portal vein alone may not necessarily be followed by congestion in zones supplied by the occluded vein. In order that these results should follow Köhler and Chiari consider that accessory circumstances must exist, such as venous congestion, decreased cardiac activity, etc. The ultimate result of these areas of congestion is not known and the shortest time in any of the cases reported in which the area of congestion occurred following the thrombosis of the portal vein was three days in a case reported by Chiari. In Case 12 the time was less than 24 hours.

True Anemic or Hemorrhagic Infarcts of the Liver Resulting from Occlusion of Smallest Interlobular Branches of the Portal Vein.

True infarcts of the liver with necrosis occur as the result of occlusion of the smallest portal vein radicals, namely, the interlobular veins. Under these conditions the blood from the hepatic artery no longer can reach the capillaries of the lobule by its anastomosis with the interlobular veins. There is then a complete mechanical deficiency of the circulation leading often to complete local necrosis of the liver parenchyma which may be combined with hemorrhage.

Cohnheim and Litten[22] emphasized the fact that if the liver parenchyma is to remain free of secondary changes, the interlobular vein must not be involved by the occluding mass. Orth[23] also said that while there may be no effect from occlusion of big branches of the portal vein, if the interlobular branch is involved atrophy as well as necrosis results. To this type of necrosis belong the well-known necrosis of eclampsia as described by Schmorrl, Klebs, Lubarsch, etc. Chiari[24] in his discussion of these infarcts includes cases described by Rattone and Mondino, and Osler. Rattone and Mondino deny the occurrence of inner portal vein radicals, and consider the entrance of the branches of the hepatic artery into the capillaries of the acini of the greatest importance. They describe two cases of infarction. In their second case the hepatic artery and portal vein were both occluded in the affected zone. This was also true in Osler's case. The liver was cirrhotic and showed a reddish-brown necrotic area on the surface which extended through the liver tissue as a triangle. The portal vein leading to this was thrombosed and Osler considered the cirrhosis to have shut off the hepatic circulation.

Chiari then adds three cases. The first occurred in a case of tuberculosis. The liver was the seat of multiple small tuberculous nodules. There were numerous thrombi in the mesenteric veins leading from the colon. Microscopically aside from the tuberculosis there were numerous interlobular veins plugged by emboli, from the mesenteric thrombi. There were also small areas of coagulative necrosis of the liver cells which Chiari considered to be infarcts. The case is not convincing.

In his second case following an operation (resection of the pylorus of the stomach) there were thrombi in the gastric and pancreatic veins. These fed small emboli to the interlobular portal branches and multiple small whitish infarcts characterized by typical coagulative necrosis resulted.

As an instance of infarction of the liver resulting from thrombosis of the interlobular veins he cites a case of eclampsia.

Ruczynski[25] adds two more cases of this type. Castigne's case in which necrotic areas occurred in the liver the result of small emboli from thrombi in the portal roots and Longcope's case where there were yellow thrombi in the hepatic vein and smallest portal veins causing yellow, necrotic infarcts in the parts supplied by the portal vessel.

Versé also describes a case of chronic perityphilitis in which the surface of the liver showed numerous pale, brown, depressed areas. On section these were dark red, soft and spongy and showed microscopically dilated vessels and necrotic liver cells. The portal vein was occluded by an old thrombus 5 cm. from the hilus, and near the infarct was a canalized fibrous thrombus. This case is of further interest since the thrombosis of the large portal root was without effect, but occlusion of the small branches brought about necrosis. The following case belongs to this group:

15. G. L., colored male, 53 years. Autopsy No. 228.

Anatomical Diagnosis.—Primary carcinoma of stomach; secondary in liver, lymph glands and pleura; chronic diffuse nephritis; nodular arteriosclerosis; *thrombosis of minute portal vessels; softened hemorrhagic infarcts of liver.*

Liver weighs 2600 grams. It is very large and contains numerous rather soft, nodular masses which vary considerably in size ½ to 7 cm. These masses project slightly above the surface and are flat and sometimes very slightly umbilicated. Some of the nodules are exceedingly soft. On section a large amount of bloody fluid escapes. This appears to come from smooth walled cavities. Some of these cavities are situated directly in the liver tissue while others are surrounded by a small amount of the tissue of the tumor. These spaces sometimes form large con-

[22] Cohnheim and Litten: *Loc. cit.*

[23] Orth: *Loc. cit.*

[24] Chiari: *Loc. cit.*

[25] Ruczynski: *Loc. cit.*

necting cavities in the liver. Some of these are filled with pure cells. In some of the larger ones thrombi are seen projecting into the cavities from minute branches of the portal vein. On further examination of these spaces in the liver they nearly all seem to be in relation to the tumors often running on one side of these. Some of the cavities are round, others very irregular, divided by numerous septa. Often the larger ones communicate. Branches of both the portal and hepatic veins especially the latter can be traced into them. On scraping the walls no epithelium was found.

An instance of peripheral zonal necrosis, similar to that occurring in eclampsia, was found in an adult male in our autopsy series. This is of interest because peripheral zonal necrosis is considered by some to be the characteristic anatomical picture of eclampsia.

OCCLUSION OF THE HEPATIC ARTERY.

The anatomy of the hepatic artery is such that firstly on account of its position at its origin from the cœliac axis it is little disposed to emboli and secondly on account of the free anastomosis of its hepatic branches with the neighboring vessels—inferior phrenic, internal mammary, superior adrenal, and the arc of vessels on the lesser curvature of the stomach—occlusion of its branches is usually without effect.

Experimental ligation of the hepatic artery varies in its results according to the animal which is used. In rabbits necroses usually result, while in dogs there is very little effect aside from a possible slight atrophy of the liver cells in the center of the lobule (Cohnheim, Litten, Whipple, etc.).

Tischner ligated the hepatic artery in 26 rabbits and in only one was there no necrosis. He says that the occlusion of the hepatic artery which is supposed only to nourish Glisson's capsule causes degeneration of the walls of the portal vein which leads to thrombosis and infarct formation. In man anemic infarcts resulting from occlusion of branches of the hepatic artery are extremely rare. To this type of infarction belong a number of cases cited by Chiari; namely, those of Obermuller, Orth, Ogle, Kaufmann, two original contributions of Chiari's, and two by Ruczynski who also cites cases by Baldwin, Heile and Bonome. Ruczynski's second case is particularly interesting for here despite thrombosis of both the hepatic artery and portal vein, the process had been so gradual that no infarct, but only a local congestion with atrophy of the liver cells resulted.

Chiari emphasized the difference between these infarcts and those resulting from occlusion of the smallest portal vein radicals. In the arterial infarct there is also necrosis of the blood vessels and connective tissue which are nourished by the hepatic artery. There are no cases of this type in our first 3500 autopsies.

OCCLUSION OF HEPATIC VEIN.

Welch [28] cites a case reported by Arnold where a condition similar to the "atrophic red infarct of Zahn" followed plugging of an hepatic vein by a retrograde embolus.

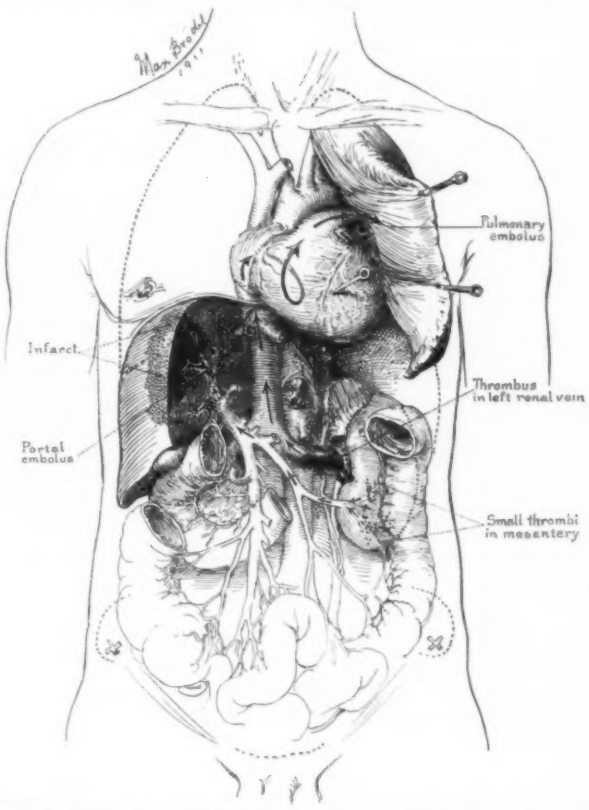
[28] Welch: Thrombosis and Embolism; Allbutt: System of Medicine, 1899, VII, 280.

In some unfinished experiments B. Bernheim and myself have almost completely ligated an hepatic vein of a dog without marked effect. The lobe of the liver a few weeks after ligation is indistinguishable from the remainder of the organ macroscopically or microscopically. This is confirmed in the following post mortem record:

F. E., white male. Autopsy No. 769. Dr. Flexner.

Anatomical Diagnosis.—Amœbic dysentery; amœbic abscess of liver penetrating into lung. Fibrino-purulent pleurisy; perforation into inferior vena cava. *Thrombosis of inferior vena cava extending into right auricle and hepatic veins.*

The inferior vena cava beginning at a point just above the rupture (of liver, abscess into cava), contains an occluding de-



colorized, firm, adherent thrombus, which extends upwards and projects into the right auricle which it about one-third fills. Some of the hepatic veins are thrombosed in part of their extent. The thrombi in the upper part are decolorized, but deeper in the liver tissue they are red and soft.

CONCLUSIONS.

1. On account of the extensive anastomosis of the intrahepatic branches of the portal vein and the hepatic artery, occlusion of either of them is usually without effect upon the liver parenchyma.

2. The portal vein may be completely occluded and the liver only appear slightly smaller and congested. In these cases an extensive collateral circulation usually establishes itself in the hepato-duodenal ligament and the portal blood is in this way carried to the interlobular vessels.

3. Following occlusion of the portal vein the entire liver, if it is the main branch, or only the part supplied by the occluded vein may present a much more congested appearance. This is due to the insufficiency of arterial anastomosis which is enough to nourish the liver cells and prevent necrosis, but which allows the blood from the systemic veins to dam back into the liver capillaries. This picture is only produced when the general circulation is impaired.

4. When the smaller interlobular branches of the portal vein are occluded the anastomosis with the hepatic artery becomes ineffectual and there is a total mechanical obstruction of the circulation in the area. This is followed by infarct formation. There is necrosis of the liver cells often accompanied by hemorrhage. The necrosis of eclampsia belongs to this group.

5. Occlusion of branches of the hepatic artery may result in true infarct formation. This is rare, firstly, on account of its peculiar position at the coeliac axis, and secondly because of its abundant anastomoses.

6. Occlusion of both the portal vein and the hepatic artery results in infarct formation unless the process is very gradual.

7. Occlusion of the hepatic vein may bring about a congestion in the zone drained by it or may be absolutely without effect.

The accompanying illustrations, kindly made by Prof. M. Brödel, illustrate very well the course of the various emboli in Case 12, and secondly the resultant wedge-shaped area of congestion following the localization of the embolus in one of the large right branches of the portal vein.

THE TEACHING OF EXPERIMENTAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY TO LARGE CLASSES.*

By Richard M. Pearce, M. D.,

Professor of Research Medicine and of Pathology, University of Pennsylvania.

The course in experimental pathology and pathological physiology here presented in outline, is an attempt to bring physiology into relation with morphology and symptomatology and thus to fill the gap which exists between the autopsy room and the laboratory of pathological histology on the one hand and the clinic on the other. Many teachers of pathology, following the lead of Cohnheim, have, it is true, introduced into their class work demonstrations illustrating some of the important problems of pathological physiology; but these have usually been perfunctory demonstrations given in a fragmentary way before the entire class, and without, as a rule, the utilization of the methods of exact registration employed in physiology. Of an entirely different character is the method which was followed for several years by Dr. W. G. MacCallum at the Johns Hopkins Medical School and is continued there along similar lines by Dr. Whipple. In this course a class of eight students worked for a period of two to three months on one organ or a group of related organs, utilizing all the methods which experimental pathology could bring to bear on the problems under consideration. The value of such a course cannot be over estimated and it should have, as an elective, a place in the curriculum of every good medical school. It has, however, the disadvantage that it cannot be given, on account of the great detail of the work, to all the members of a large class and must remain essentially an elective course combining instruction and research for a small number of students.

For a long time, it has seemed to me desirable that a course in experimental pathology should be developed which, while including as far as possible valuable features of MacCallum's "small group" course, should at the same time be so arranged as to be available to all the members of a large class. Amphitheatre demonstrations are not advisable, as only the few men close to the demonstration table benefit by such procedures. Likewise individual work by the student, such as is now given in our better courses in experimental pharmacology, is out of the question, for the present at least, on account of the lack of equipment and space in most of our laboratories of pathology. The course which I have given during the latter half of the past academic year has been a compromise between these two methods, in that, although the demonstration method has been used, the number of demonstrations in one period has been sufficient to break up the class into small groups. Thus a class of 90 men has been divided into two sections, each section meeting, during 14 weeks, once a week for one hour. At these sessions at least five demonstrations, each under the direction of a member of the department, have been presented simultaneously. Thus each section of 45 men was subdivided into five groups of 9 men, and each of these had at least 12 minutes for a demonstration. The room in which the course was given was of a size sufficient to allow a wide space between the demonstration tables, and also to allow the passage of groups from table to table, on signal, without confusion.

The general scope of the course was based in part on Cohnheim's classical experiments, MacCallum's course at Hopkins, Rous' course at Michigan, Longcope's elective course in "medical correlation" given last year at this school and the demonstration courses to physicians given for several years in the Medical Department of Columbia University, and in part on an extensive personal acquaintance with the methods of experimental pathology and their possibilities. The course is not to be considered as complete or perfect, or as in every way ideal, but rather as a tentative summary of what has, in my hands, proved most satisfactory in the instruction of large classes. The possibilities of enlarging its

* Read before the International Association of Medical Museums, Chicago, April 13, 1911.

scope and of improving its presentation are numerous and will be evident to any one familiar with the methods of physiology and chemistry as applied to experimental pathology.

The following outline is a copy of the mimeographed sheets given each member of the class two days before the demonstrations:

EXERCISE I.

BLOOD DESTRUCTION AND JAUNDICE.

Table I. (a) Rabbit which received, three days before demonstration, 0.001 gm. rattlesnake venom in ear vein. Note *hemoglobinuria*, the result of the hemolytic action of snake venom.

(b) Dog which received, three days before demonstration, 0.2 cc. of hemolytic immune serum per kilo of body weight in saphenous vein. Note *hemoglobinuria* (and jaundice ?).

Table II. Experiments *in vitro* explaining phenomena seen above *in vivo* (hemagglutination and hemolysis).

Table III. (a) Rabbit which received, 24 hours before demonstration, 0.001 gm. cantharidin in acetic ether, subcutaneously. Result: *Free blood in urine* (hematuria), *not hemoglobinuria*—equivalent to a hemorrhagic nephritis.

(b) Microscopic preparations showing the sediment of the urine of (1) *hematuria* (red blood corpuscles present) and (2) *hemoglobinuria*.

Table IV. (a) Dog with *jaundice*, the result of the ligation of the common bile duct for three days. Note skin, conjunctiva and urine.

(b) Tests for bile in urine of Ib and IVa.

Table V. (a) Test for albumin in urine of Ia, Ib, IIIa, IVa.

(b) Spectroscopic test of urine of Ib.

(c) Microscopic sections illustrating the changes in the various organs of the above animals.

EXERCISE II.

DEGENERATION AND NECROSIS.

Table I. (a) Rabbit: Gross demonstration of *cloudy swelling* due to repeated injections of cantharidin in ether.

(b) Microscopic preparations of liver and kidney treated with salt solution and acetic acid.

Table II. (a) Rabbit: *Fatty changes* due to poisoning by phosphorus.

(b) Microscopic preparations treated by acetic acid, Sudan III and osmic acid.

Table III. (a) Dog: *Necrosis* from loss of blood supply. Ligation of superior mesenteric artery and one branch of renal artery.

(b) *Gangrene* in guinea pig's leg secondary to ligation of femoral artery and vein.

Table IV. (a) Rabbit: Illustrating gas formation in *emphysematous gangrene*. Injection of *B. aerogenes capsulatus* in ear vein; animal then killed and placed in thermostat at 37.5° C. for 24 hours.

(b) Microscope with preparation of *B. aerogenes capsulatus*.

Table V. (a) Guinea pigs showing *caseation* of tuberculosis. Four weeks after injection of bovine tubercle bacilli into peritoneal cavity.

(b) Microscope with preparation of *B. tuberculosis*.

EXERCISE III.

INFLAMMATION AND REPAIR.

Table I. (a) Ear of rabbit exposed to water at 56° C. for three minutes—condition after 24 hours.

(b) Ear of rabbit 24 hours after rubbing with croton oil.

(c) Microscopic preparations illustrating histology of each.

Table II. (a) Rabbit: *Pleuritis* due to injection of aleuronat, 48-hour lesion.

(b) Ditto due to injection of turpentine, 48-hour lesion.

(c), (d) } Microscopes with exudate from { (a), (b)

Table III. (a) Rabbit: Multiple *embolic abscesses* resulting from injection of staphylococcus pyogenes aureus in ear vein. 48-hour lesion.

(b) Microscopic preparations illustrating lesion in kidney.

Table IV. Dog: *Repair* of *aseptic wound*, 3 days.

Table V. Dog: *Repair* of *infected wound*, 3 days.

Compare carefully gross appearance of Ia and Ib.

Compare carefully gross appearance of IV and V.

EXERCISE IV.

THROMBOSIS, EMBOLISM, INFARCTION.

Table I. Rabbit: *Multiple bland infarctions* due to embolism produced by injection of foreign particles (tobacco seed). (Compare with multiple embolic abscesses due to injection of *Staphylococcus pyogenes aureus*, as seen in last weeks' exercise.)

Table II. Dog: *Air embolism* with graphic registration of changes in blood pressure, heart action and respiration. Ether anesthesia. Autopsy showing method of demonstrating air in heart cavities.

Table III. (a) Dog: *Thrombus* in jugular vein resulting from injury to intima caused by mechanical pressure.

(b) *Thrombus* formation in ligated artery (femoral).

Table IV. Sections of liver and spleen showing *hyalin thrombi* composed of agglutinated red blood corpuscles. From dog which received hemolytic (also hemagglutinative) serum (see Exercise I) and died after one hour; also sections from animals similarly treated, showing necrosis of the liver after twenty-four hours.

EXERCISE V.

HEART.

(All experiments under ether anesthesia.)

Table I. *Hydropericardium:* Experimental condition produced by introducing a large amount of salt solution into the pericardial cavity. Graphic registration of effect on heart action and arterial and venous pressure. Artificial respiration.

Table II. *Myocarditis:* Production of myocardial insufficiency by injection of alcohol into heart substance. Graphic registration of effect on heart action and blood pressure.

Table III. *Valvular Insufficiency:* Mechanical rupture of aortic valve by instrumentation through carotid artery. Graphic registration of effect on heart action and blood pressure.

EXERCISE VI.

LUNGS.

(All experiments under ether anesthesia.)

Table I. Graphic registration showing effect of double *Hydrothorax* on respiration, heart action and blood pressure. Hydrothorax produced by injection of salt solution.

Table II. Demonstration of the anatomical relations in the thorax under above conditions, *Atelectasis*.

Table III. *Emphysema:* The lungs of a guinea pig in the experimental condition known as anaphylaxis. The gross appearance of the lungs is similar to that of emphysema.

Table IV. (a) "*Deglutition*" *pneumonia;* due to foreign particles in bronchi.

(b) *Purulent pleuritis* (empyema) due to *Staphylococcus pyogenes aureus*.

Table V. *Edema of lung;* produced by infiltration of lung with salt solution. Graphic registration of effect on heart, blood pressure, and respiration.

EXERCISE VII.

STOMACH AND INTESTINE.

Table I. Experimental *Toxic gastritis*, due to (a) carbolic acid and (b) corrosive sublimate.
Table II. Experimental *Toxic gastritis*, due to (a) sulphuric acid and (b) nitric acid.
Table III. Experimental *Toxic gastritis*, due to caustic alkali (sodium hydrate).
Table IV. Experimental *Peptic ulcer*, produced by injecting serum beneath mucosa and by excising small portion of mucosa.
Table V. *Intussusception* and *Volvulus* of Intestine and *internal hernia.*
(All lesions produced under ether anesthesia followed by death from chloroform.)

EXERCISE VIII.

PANCREAS.

Table I. Hog: Acute *hemorrhagic* and gangrenous pancreatitis and *Fat necrosis* following injection of bile into pancreatic duct. Lesions of twenty-four hours and forty-eight hours respectively.
Table II. Ligation of duct for period of two months; slight *atrophy;* no glycosuria.
Table III. *Experimental Diabetes* following extirpation of pancreas.
Table IV. *Phloridzin Diabetes.*
Table V. Tests for sugar in the urine of all of above.

EXERCISE IX.

LIVER.

Table I. Multiple focal necroses of liver due to the injection of hemolytic and hemagglutinative immune serum.
Table II. Necrosis of liver due to prolonged inhalation of chloroform.
Table III. Obstructive Jaundice.
Table IV. Demonstration of a "spontaneous" cirrhosis of the liver in the dog.
Table V. (a) Sections illustrating microscopic picture in above lesions.
(b) Tests illustrating changes in the urine in I, II, and III.

EXERCISE X.

KIDNEY.

Table I. Acute nephritis in rabbit due to injection of 0.06 gm. potassium chromate. Essentially a tubular injury. 48 hours.
Table II. Acute nephritis in rabbit due to injection of 0.05 mg. rattlesnake venom. Essentially a vascular nephritis. 48 hours.
Table III. Acute nephritis with *edema* in rabbit. Due to injection of uranium nitrate and the administration of an excess of water by stomach tube. 5 days.
Table IV. Demonstration of factors influencing vascular reactions and diuresis in experimental nephritis. Oncometric studies.
Table V. (a) Urine of each of above showing albumin and casts.
(b) Stained sections of similar lesions.
Table VI. Hydronephrosis. 6 weeks after ligation of one ureter.

EXERCISE XI.

HYPERSUSCEPTIBILITY (Allergy).

Table I. *Peculiar natural hypersusceptibility* to rabbit effluvia and to rabbit serum in case of a human patient.
Table II. *Experimental anaphylaxis:*
(a) Morbid anatomy and histology of the lungs of anaphylactic guinea pig.
(b) Physiology of anaphylactic "shock" in dog.

IMMUNITY.

Table III. *Combination of toxin and anti-toxin:*
(a) Guinea pig injected with diphteria toxin; (b) guinea pig injected with diptheria toxin and protected by anti-toxin; (c) control animal injected with anti-toxin alone.
(d) Similar series with tetanus toxin and anti-toxin.
Table IV. (a) *Agglutination* of bacteria and of blood cells by specific immune sera.
(b) *Precipitation* of dissolved proteins by specific immune sera.
Table V. *Cytolysis:* (a) Hemolysis by means of specific immune sera in high dilutions, by natural hemolysins and by hematoxic agents, e. g., rattlesnake venom.
(b) *Fragility* of erythrocytes as shown by the use of salt solutions of varying tonicity.
Table VI. *Complement Fixation:* (a) Phenomenon with precipitins and other immune sera.
(b) Wasserman reaction.

EXERCISE XII.

DUCTLESS GLANDS. INTERNAL SECRETION.

Table I. Local Vaso-constrictor effect of adrenalin as seen in rabbit's ear.
Table II. Effect of adrenalin on blood pressure as seen in dog.
Table III. Adrenalin glycosuria. Rabbit.
Table IV. Result of extirpation of adrenals. Dog.
Table V. Effect of extracts of hypophysis on blood pressure and diuresis, as seen in dog.
Table VI. Tetany in parathyroidectomized dog.
Table VII. Effect on tetany of injection of a calcium salt.
Table VIII. Review Exercise VIII, Demonstration III, Result of extirpation of pancreas.

EXPERIMENTAL PATHOLOGY AND PHYSICAL DIAGNOSIS.

EXERCISE XIII.

(In collaboration with Dr. W. T. Longcope.)

(All dogs under ether anesthesia and with tracheal canula, artificial respiration and mechanical ether dropper.)
Table I. *Normal dog:* By percussion and auscultation, note normal physical signs of respiration and the outlines of the lungs.
Table II. *Pneumothorax:* Normal dog. Note changes in physical signs produced by injection of air (200 cc.) into pleural cavity.
Table III. *Hydrothorax:* Due to injection of 400 cc. normal salt solution into pleural cavity. Note change in level of dullness on altering position of dog and of percussion notes and respiratory sound above and below level of fluid.
Table IV. *Acute Pleuritis:* Right side, 3 cc. turpentine injected into pleural cavity one hour before demonstration. Left side, same amount injected at beginning of demonstration. Compare friction rubs on both sides.

Table V. *Edema:* Bronchitis due to introduction of irritating substance as turpentine or ammonia into trachea. Study râles.

At autopsies on the above animals note:

Table I. Collapse of lungs and their position in relation to thoracic wall. Appearance of pleural surface.

Table II. Clamp tracheas before opening thorax, note condition of lungs.

Table III. Clamp tracheas, note level of fluid and compare with level determined by percussion. Note compression of lungs.

Table IV. Note amount and character of exudate on each side and appearance of pleura.

Table V. Note condition of bronchi; look for sclerosis and congestion.

(In connection with above, review Exercise VI.)

EXERCISE XIV.

(In collaboration with Dr. W. T. Longcope.)

(All dogs under ether anesthesia with tracheal canula, artificial respiration and mechanical ether dropper.)

Table I. *Normal dog:* Note normal heart sounds, over different regions of thorax. By palpation and percussion note area of cardiac dullness.

Table II. *Normal dog:* Thorax and pericardium opened. Note action of heart. Study heart sounds by auscultation directly over various regions of heart.

Table III. *Aortic regurgitation:* (a) Aortic cusp destroyed by instrumentation through left carotid artery. Note changes in heart sounds and cardiac dullness. (b) Same with thorax and pericardium opened; direct auscultation.

Table IV. *Aortic stenosis:* Thorax and pericardium opened. Aortic stenosis produced by tightening ligature about base of aorta. Note heart sounds and changes in shape, size and position of the various chambers of the heart.

(In connection with above, review Exercise V.)

These demonstrations, it is seen, include the presentation of necrosis and the degenerations, inflammation and repair, blood destruction and jaundice, thrombosis, embolism and infarction, certain lesions of the heart, lung, stomach, intestines, liver, pancreas, and kidney, and the problems of infection and immunity, of shock and hemorrhage and the physiology of the ductless glands.

With the exception of Exercises II, III, IV, XI, the experimental work was presented in connection with the general pathology and pathological histology of the subject under consideration. Physiological methods of graphic registration were used whenever possible; changes in the urine and other secretions demonstrated; and the methods of chemical diagnosis emphasized.

The planning of the course is no small matter and the labor of preparation * is great, but the actual demonstrations are not difficult; even if they were, the change in the attitude of the student toward pathology, which such a course brings about, makes it well worth while. This is particularly true of Exercises XIII and XIV which, given in collaboration with Dr. W. T. Longcope as a part of the course in Physical Diagnosis, were received with the greatest interest. To let the student produce, or see produced, certain anatomical lesions, and to allow him to study the alterations of function which result, applying thereto many of the clinical methods, and eventually at autopsy to correlate the disturbances in physiology with the anatomical changes, is, I believe, a most valuable preparation for clinical study in that it bridges the gap between pathological anatomy and clinical observation. Herein lies the chief value of courses in experimental pathology and pathological physiology.

* The success of this course, as given during the past year, is due in largest measure to the efforts of my assistants, Drs. A. B. Eisenbrey, H. T. Karsner, B. S. Veeder, and J. H. Austin, upon whose shoulders fell the burden of preparation.

A PROTEST AGAINST THE INDISCRIMINATE USE OF THE ORGANIC COMPOUNDS OF SILVER IN OPHTHALMIC PRACTICE.*

By SAMUEL THEOBALD, M. D.,

Clinical Professor of Ophthalmology and Otology, The Johns Hopkins University.

Whatever be the explanation, whether due to their chemical composition, the greater freedom with which they are used, or to their supposedly greater penetrating power, there can be no doubt that the organic compounds of silver—at all events, those with which I am familiar, protargol and argyrol—are responsible for many more cases of conjunctival argyria than ever was, or is, silver nitrate.

Before these compounds came into use, argyria of the conjunctiva was a rare condition—practically never seen except in old cases of trachoma. Now, it is relatively common, and is met with not only in chronic conditions, such as trachoma, but in acute affections as well, in which the silver treatment has been of comparatively brief duration.

I believe I am warranted in saying that I have never produced a case of ocular argyria from the use of silver nitrate. I regret that I cannot say the same as to the newer silver compounds. In several of my cases of gonorrhœal conjunctivitis in the adult decided staining, especially of the bulbar conjunctiva, has resulted from the employment of protargol, and the same has happened in a case of acute trachoma after only a few weeks treatment.

I have also observed a number of cases of similar character which have occurred in the practice of my confrères. A well-known physician of Baltimore was given a five per cent solution of argyrol for a mild chronic conjunctivitis. As its action was beneficial, his wife—in need only of glasses for the correction of a decided fault of refraction—also began to use it, and the two continued to employ it, p. r. n., until the physician had acquired one of the most marked cases of

* Read before the American Ophthalmological Society, July 11, 1911.

argyria I have ever seen, and his wife's eyes had become conspicuously stained.

Let me make it plain, that I have no unreasoning prejudice against these newer silver preparations. On the contrary, I have such faith in protargol, especially, that for some years I have employed it in the treatment of gonorrhœal conjunctivitis, both in the infant and the adult, to the exclusion of silver nitrate, and in trachomatous conjunctivitis, especially in the acute stage, it has also been my chief reliance.

It is, therefore, not against the *use*, but against the *indiscriminate*—or, perhaps, I might say indiscriminating—use of the organic silver compounds that I would protest. When a remedy is at hand, that is, at least, as efficacious as they are in the condition to be dealt with, that is cleanly and that cannot by any possibility produce the untoward consequences to which, as has been pointed out, they not rarely give rise, common sense would seem to dictate that it be given the preference.

These observations apply with especial force to the now almost, it would seem, universal habit, particularly among the younger generation of ophthalmologists and of general practitioners, as well, of employing argyrol or protargol, in the treatment of acute and chronic catarrhal conjunctivitis. This practice, in my judgment, and it is based upon abundant observation, is wholly indefensible, since we have a remedy—in a collyrium containing half a grain of zinc sulphate and ten or twelve grains of boracic acid to the ounce—that is cleanly, and that is not simply *as* efficacious, but is more surely and more promptly efficacious in these conditions than either of the silver compounds mentioned.

NOTES ON JAUNDICE IN PNEUMONIA.

By Fletcher McPhedran, M. B.,

Assistant Resident Physician, The Johns Hopkins Hospital.

Since Bettelheim and Leichtenstern first reported the occurrence of jaundice in lobar pneumonia, many explanations of its pathology have appeared in the literature. Bouillaud considered it due to a transfer of the infection to the liver; Niemeyer to pressure of the hepatized lung on the torpid liver; Virchow and Leyden to an associated duodenal catarrh resulting in simple jaundice.

Banti[1] thought it due to a specific hæmolytic action of the diplococcus pneumoniæ, probably general in its distribution but maximal in the spleen. He found that hæmoglobinuria occurred in rabbits after infection with the pneumococcus. This hæmoglobinuria was not an index of the virulence of the germ, but was caused by a pneumococcus that had produced jaundice in man. In dogs he produced bilirubinuria, and concluded that in man the pneumoccoccus produced bilirubin which was changed in the tissues to urobilin, causing jaundice, and was excreted as urobilin.

Obermayer and Popper[2] investigated 134 cases of pneumonia, demonstrating pathological amounts of pigments (bilirubin, urobilin and biliverdin) in all urines, and found that these pigments had been described as urobilin, because the tests employed had not been sufficiently accurate to differentiate them. When the pigments were present in sufficient quantities to give the less delicate tests, jaundice appeared. They considered the jaundice hæmolytic and dependent upon the intensity of the infection. At autopsy they found large quantities of pigments in the hepatized and slight amounts in the congested areas, but felt that the color might be due to the pigments in the serum of the affected regions.

Herzfeld and Steiger[3] found pigments with great difficulty or not at all in the urines of patients whose sputa readily yielded them. As the pigments were only found when blood was mingled in the sputum, they concluded that they came from the extravasated red blood cells of the hepatization, and *in vitro* were able to show that the pneumococcus produced from hæmoglobin a body giving the color reactions of bilirubin.

Troisier[4] had meanwhile described the icterus as due to this local destruction, comparable to that observed in hæmorrhagic pleurisy, where diminished corpuscular resistance to hypotonic sodium chloride solutions is found, and where the bile pigments are produced apart from the liver. From this local area of destruction the pigments are carried throughout the body.

Lemierre and Abrami[5] found in two cases pure culture of the pneumococcus in the bile associated with no obstruction, but a definite degeneration of the liver cells. They thought all pigment must come from the liver.

It seemed that it might be a matter of interest to estimate the corpuscular resistance in a series of cases of lobar pneumonia with and without jaundice, in order to determine the question as to whether any of these cases might show a diminution of corpuscular resistance. During the last winter fourteen cases have been examined. The corpuscles were tested against solutions of chemically pure sodium chloride, progressively diminishing in strength from 0.6 per cent down to 0.26 per cent. The blood was received into a citrate solution in 0.85 per cent sodium chloride, washed three times with sodium chloride solution, and then the sedimented corpuscles dropped into tubes, each of which contained 3 cc. of the hypotonic sodium chloride solution. After two hours at 37 degrees C., the tubes were placed on ice and examined again after twenty-four hours. All glass ware was kept clean and the solutions sterile. Three readings were made, at the point of initial, marked and complete hæmolysis. Normally, initial hæmolysis should be at 0.42 per cent, marked at 0.34 per cent and complete at 0.26 per cent.

The urine was tested for urobilin, but in no case was there

any pathological increase. If the red blood cell counts were constant, one would expect a large number of new cells, which could be discovered by vital staining as described by Vaughan.[6] There was not any increase of the number of red blood cells so stained.

PNEUMONIAS WITHOUT JAUNDICE.

Name.	Race.	Sex.	R. B. C.	Initial.	Marked.	Complete.
1-G.	C.	F.	5,200,000	40	36	30
2-C.	W.	M.	5,232,000	42	36	32
3-C.	W.	M.	5,416,000	44	36	28
4-T.	W.	M.	3,300,000	42	36	32
5-G.	W.	M.	5,300,000	50	40	38
6-B.	W.	M.	4,900,000	44	36	30

PNEUMONIAS WITH JAUNDICE.

Name.	Race.	Sex.	R. B. C.	Initial.	Marked.	Complete.
7-J.	C.	F.	4,500,000	30	28	26
8-T.	C.	M.	4,704,000	38	34	26
9-S.	C.	M.	4,300,000	40	34	26
10-H.	W.	F.	5,250,000	40	34	28
11-J.	W.	F.	4,080,000	42	34	30
12-H.	C.	M.	5,280,000	44	38	30
13-F.	C.	M.	5,300,000	36	30	26
14-M.	W.	M.	4,800,000	38	32	26

Case No. 5 is noteworthy in view of the increased fragility of the cells found, but attempts to follow up the patient outside the hospital have been unsuccessful. He was not in the least jaundiced and showed no increase in reticulated cells.

It is interesting that in cases Nos. 7, 8 and 13, where clinically the jaundice was most intense, and bile pigments were readily found in the urine, the fragility was diminished, that is, the same condition obtained as was described by Chalier in obstructive jaundice.

The use of saponin (Merck's "purissimum") for hæmolysis as advocated by McNeill[7] was also tried, but the results in a series of control cases were not sufficiently accurate to warrant its continuance. He took a suspension of washed corpuscles in such an amount that there were about 50,000,000 cells, to which varying amounts of a saponin solution of 0.004 gm. to 100 cc. of 0.85 per cent sodium chloride were added. Then the mixture was brought to a volume of 2 cc. by more of the same sodium chloride solution and the number of red blood cells were counted on a Thoma Zeiss hæmocytometer. After incubation at 37 degrees C. for two hours, the remaining cells were enumerated and the amount of hæmolysis observed.

NORMAL ADULT.

Tube No.	R. B. C. suspension in NaCl 0.85 per cent.	Saponin.	NaCl 0.85 per cent.	Corrected Number R. B. C.	R. B. C. after 2 hours.	Per cent. of Hæmolysis.
	cc.	cc.	cc.			
1	.15	.08	1.77	43,000,000	41,700,000	46
1a	.15	.08	1.77	50,500,000	34,500,000	32
2	.15	.12	1.73	42,000,000	28,000,000	33
2a	.15	.12	1.73	41,200,000	27,600,000	34
3	.15	.16	1.69	42,000,000	28,000,000	33
3a	.15	.16	1.69	41,200,000	36,400,000	08
4	.15	.2	1.65	42,000,000	31,000,000	26
4a	.15	.2	1.65	40,300,000	26,200,000	35
5	.15	.24	1.61	42,000,000	1,000,000	97
5a	.15	.24	1.61	42,000,000	24,600,000	41

PNEUMONIA WITH JAUNDICE.

Tube No.	R. B. C. Suspension in NaCl 0.85 per cent.	Saponin.	NaCl 0.85 per cent.	Corrected Number R. B. C.	R. B. C. after 2 hours.	Per cent of Hæmolysis.
	cc.	cc.	cc.			
1	.13	.1	1.77	46,700,000	36,000,000	21
2	.13	.2	1.67	55,600,000	25,000,000	54
3	.13	.3	1.57	54,000,000	29,000,000	46

Now we see in the above that the same experiment repeated with the same technique on one individual gives widely variant results; for example, compare tubes 3 and 3a and tubes 5 and 5a. Nevertheless, there is a very slight, if any, difference in the figures of hæmolysis in the case of jaundice in pneumonia and in the normal adult.

Two cases, Nos. 7 and 8, came to autopsy; in neither was there any obstruction to the bile ducts, nor any destruction of liver cells, nor any increase in pigment found by the usual methods.

The number of red blood cells on admission was interesting; it averaged 4,840,000 for the males with jaundice and 4,400,000 for the females. In cases without jaundice, the number was 4,800,000 in males, and 5,200,000 in the only female. A series of typhoid fever patients comparable in age and duration of disease to this pneumonia series averaged 5,900,000 for males and 4,500,000 for females.

From the fact that the cells are in the lungs in such numbers, and that the pneumococcus has definite hæmolytic powers, together with the property of producing bile pigments, it is probable that the jaundice arises from the pigments produced in the lungs; but as all patients with pneumonia have this extravasation, there must be some other cause, perhaps a variation in the pneumococcus. This is not associated with the general increase in the fragility of the red blood cells.

SUMMARY.

1. In the fourteen cases there was increased fragility in only one case, this without jaundice; but in the cases with most marked jaundice there was, on the contrary, an increase in the corpuscular resistance.

2. The urine in no cases showed any excess of urobilin.

3. Bilirubin was present in the urine in three of the eight cases with jaundice.

4. Autopsy showed no evidence of special changes in the liver.

5. The blood counts showed such a loss that one must consider it as due to a sudden great destruction. This loss is probably due to the hepatization.

In concluding, I desire to thank Dr. W. S. Thayer for constant advice and assistance.

BIBLIOGRAPHY.

1. Banti: Centralbl. f. Bakteriol. und Parasitenk., 1896, XX, 849.
2. Obermayer and Popper: Wien. klin. Wchnschr., 1908, XXI, 895.
3. Herzfeld and Steiger: Med. Klinik, 1910, VI, 1415.
4. Troisier: Compt. rend. Soc. de biol., 1909, LXVIII, 46.
5. Lemierre and Abrami: Presse méd., 1910, XVIII, 82.
6. Vaughan: J. M. Research, 1903, V, 342.
7. McNeill: J. Path. and Bact., 1910, XV, 56.

ABDOMINAL LIPECTOMY.

REPORT OF TWO CASES.

By W. F. Shallenberger, M. D., Atlanta, Ga.,

Late Resident Surgeon, Maryland Hospital for Women, Baltimore.

This operation,[1] while no longer rare, is uncommon enough to warrant the report of these two cases, which came under my care at the Woman's Hospital in Baltimore.

Mrs. S., age 39, was sent to the hospital by her physician in March, 1910, for symptoms of a chronic appendicitis from which she had suffered for several years and which had been becoming more aggravated. She had a more or less constant pain in the right lower quadrant of the abdomen, which was quite severe at times. There was also nausea and vomiting occasionally, and constipation. No history of jaundice or

Fig. 1.

Fig. 2.

Fig. 1.—Healed incision in first patient showing the support the umbilicus gives. (Patient is standing.)
Fig. 2.—First patient, showing the abdominal supporter worn after operation.

urinary disturbance was obtained. The menstrual history was negative. The patient had had several children. Backache was the only symptom that suggested any pelvic trouble.

Eight years ago the patient had an attack of typhoid fever, after which she began to grow very stout. Prior to this attack she had been of average size.

Examination.—The patient was quite fat, weight 227 pounds, of medium height. The outlines of her figure were good, except of the abdomen, which was very full and flabby, with a regular apron of fat that hung down over the symphysis when the patient was standing. One could pick the fat up in a great ridge or fold across the lower abdomen. The greatest deposit of fat was below the umbilicus, and it prevented the wearing of an abdominal supporter because of the flabbiness. The abdominal walls were firm beneath the fat.

On the right side there was tenderness over the appendix region, with slight muscle rigidity. The temperature was normal. The pelvic organs were normal except for a slight laceration of the cervix uteri and a moderate relaxation of the perineum. The backache I thought was due to the pendulous abdomen.

The patient received the suggestion that some of the fat be removed with much enthusiasm and was very eager that the operation be performed.

Operation.—A double incision was made from flank to flank below the umbilicus and embracing an elliptoid area of skin 45 cm. or 18 inches long, and 15 cm. or 6 inches at the widest part. The incisions were carried down to the fascia

Fig. 3.—The slab of skin and fat removed in the second case.

and the wedge or slice of skin and fat removed. Its weight was a trifle over 7 pounds.

All the bleeding points were carefully secured and the fat of the two sides of the open area was brought together with a number of double figure-of-eight catgut sutures. The skin edges were then approximated. Three silver-wire sutures were first placed, and silkworm gut used to complete the approximation. Four rubber tissue drains were inserted, one in each angle of the incision and the others midway between the angles and the median line. These drains were removed on the third day.

Before the incision was closed, the peritoneal cavity was opened on the right side by a McBurney incision through the muscles and fascia and the appendix removed. It was large, injected and adherent.

The incision, which was 18 inches long, healed nicely and the patient had a rapid convalescence. She was greatly relieved, not only of the appendix symptoms but also of the backache. I have seen her a number of times since, and she is highly pleased with the results. We had an abdominal supporter made for her and this fits perfectly now. (Fig. 2.)

Mrs. P., a patient of Dr. Kelly, came to the hospital in

[1] Kelly, H. A.: Excision of the Fat of the Abdominal Wall—Lipectomy, Surg., Gyn., and Obst., 1910, X, 229.

December, 1910. She had a postoperative ventral hernia through an old midline incision. A hysterectomy had been done several years ago, and the patient had an incision infection and a peritonitis following. Aside from the hernia there were also extensive intestinal adhesions giving rise to considerable abdominal pain. There was a considerable deposit of fat in the abdominal wall.

Operation.—A double transverse incision was made from flank to flank, 38 cm. long and the two lines 12 cm. apart in the median abdominal line. The slab of fat was removed (Fig. 3) and the peritoneal cavity opened through the hernial sac. The intestinal adhesions were all separated and the hernia repaired by overlapping the fascia in the mid-line. The fat and skin edges were then brought together in much the same manner as in the first case, silkworm gut alone being used for the skin. Cigarette drains were placed in each angle of the incision.

The patient made an uneventful recovery and left the hospital greatly benefited by the operation.

In neither of these cases was there an umbilical hernia, and I wish to bring out a point here; namely, that where there is not an umbilical hernia the incisions should be made below the umbilicus, leaving it as a supporting point. This is shown in Fig. 1, where the highest point of the incision, as the patient stands, is seen to be in the median line below the umbilicus, and there is a tendency for the incision to sag down on each side.

Dr. Kelly did the first operation of this kind in 1899.[2] Since then he has had eight more cases, including the one reported here.

Maylord[3] reports three cases in which he did extensive lipectomy in fat women with umbilical herniæ. The first of his cases was done in 1903, and ten pounds were removed.

Weinold[4] reports a case in a woman with an enormously fat abdomen.

The results of such an operation are, to quote Dr. Kelly: "The removal of a slab of fat and a decrease in weight. Great addition to personal comfort generally. Convenience and comfort in dressing. Better pose in standing and better poise in walking. Increased activity. Cleanliness greatly facilitated. Figure changed from unsightly and awkward to one much more natural. The sensitive patient occupying afterwards a more normal and natural relation to society."

[2] Kelly, H. A.: Excessive Growth of Fat, Johns Hopkins Hosp. Bull., 1899, X, 197.

[3] Maylord, A. E.: Direction of Abdominal Incisions, Brit. M. J., 1907, II, 895.

[4] Weinold: Bauchdeckenplastik, 1909, XXIII, 1332.

IN MEMORIAM.

DR. CHRISTIAN ARCHIBALD HERTER.

In response to an invitation issued by the President of the Johns Hopkins University and the committee on the Herter Memorial Lectureship a meeting in memory of the late Dr. Christian Archibald Herter was held in the lecture room of the Physiological Laboratory of the Johns Hopkins University on Thursday, October 5, 1911, at 3 p. m.

Drs. W. H. Welch, W. S. Halsted, and J. J. Abel of Baltimore and E. Dunham and Simon Flexner of New York, spoke of various aspects of the life and work of Dr. Herter and paid tribute to his character and his services to medical science.

The following minute was adopted and was subsequently read to the audience assembled at four o'clock to hear Professor Kossel's second Herter lecture, who expressed their respect and approval by a rising vote:

MINUTE

The medical faculty and other members of the Johns Hopkins University, as well as all assembled at the delivery of the sixth series of lectures upon the Herter Foundation, desire to place upon record their sense of the great loss sustained by American Medicine and by medical science in the death of Dr. Christian Archibald Herter on December 5, 1910.

The initiation of Dr. Herter's fruitful activity as a scientific investigator by his work as a graduate student in this University and his active interest in the development of this medical school are sources of especial gratification to the University. Upon this occasion especially we recall with grateful appreciation his generous benefaction in founding, in association with Mrs. Herter, a lectureship which has been and will continue to be a fountain of inspiration and instruction to our faculty and students and to the medical profession.

In the life and work and character of Dr. Herter we recognize the manifestation of rare gifts of intellect and of heart and high-minded devotion to the highest ideals of our profession and of scientific medicine. By valuable contributions to knowledge, by wisely directed and generous material aid in the promotion of medical and biological science, by judicious counsel and active effort and by the widely felt influence of a richly endowed and singularly attractive and cultivated personality, Dr. Herter rendered memorable service to American medicine in behalf of higher professional standards and wider recognition and cultivation of medical science.

In this University and elsewhere the memory of Christian Archibald Herter will be cherished not only as that of a generous benefactor, but also "as a presence to be felt and known" exemplifying love of beauty, broad humanity and loyalty and devotion to the best ideals of the physician and the student of man and of nature.

We desire to express our sympathy with Mrs. Herter and her children in their bereavement and that a copy of this minute be transmitted to them.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XXII is in progress. The subscription price is $2.00 per year in the United States, Canada, and Mexico; foreign subscriptions $2.50.

NOTES ON NEW BOOKS.

The Principles of Pathology. By J. George Adami, M. D., etc. Vol. I. General Pathology by J. George Adami; Vol. II. Systemic Pathology by J. George Adami and Albert G. Nicholls, M. D., etc. Second Edition. Revised and Enlarged. Illustrated. (*Philadelphia and New York: Lea & Febiger. 1910.*)

This is not a new book, but is already in its second edition, so that there can be no question as to its value in satisfying a general need. The scope of such a book should be determined to some extent by the requirements of those for whom it is intended, and if any criticism is to be offered upon a text-book such as this, which is designed for the use of students as well as physicians, it is that here an attempt is made to cover in some way the whole field of pathology, including the fields of those subjects which are preparatory in a sense to the study of pathology, and upon a knowledge of which pathology depends. This encyclopædic plan has resulted in the production of two great volumes each of about a thousand pages, which are really more than the students in our schools of medicine can read and master in their course in pathology. It is perfectly true that, were the courses in pathology commensurate with their importance to the future physician as the foundation of his thought and action, he might readily require even more. For the practising physician who wishes to refer to a text-book of pathology these two volumes are excellent; but it is for the leisurely pathologist who sits down to peruse the new book that it—at least the first volume—affords pleasure. The second volume is a collaboration and in it the attempt appears to be made to apply the general principles to all the tissues and organs—an attempt which often leaves the impression given by the perfunctory fulfillment of a task, and which leads to an endless repetition of ideas which comes sometimes to involve the illustrations.

The prime effort is expended, apparently, upon the discussion of general pathological principles which, as everyone must agree, are rightly limited to those which affect all the tissues, and such things as the disturbances of the circulation which are so commonly treated as general pathological processes, are relegated to the chapters on the pathology of the circulation. In this way the general pathology becomes the pathology of the cell at large, its nutrition, its growth, its various activities and reactions to outward influences, and its transmission of its own characters.

In order to discuss all these things intelligibly, Dr. Adami occupies 200 pages with the normal anatomy, physiology, and chemistry of the cell, which then leads him to the problems of heredity. All this is very clearly written and deals with the more modern views of the changes which go on within the cells under more or less normal conditions. The treatment of the various causes of disease is superior to that in most books, in that he spends less space upon the minute descriptions of every kind of bacterium and animal parasite—things which can be studied to far greater advantage in special books on these subjects. Two or three of these chapters are devoted to a general review of malformations—again a subject of such enormous proportions that any general pathologist is wise to treat it summarily. The next section which discusses inflammation with fever and immunity is admirable, as one might expect from Dr. Adami's previous monograph upon inflammation. In speaking of repair, hypertrophy, regeneration, etc., he refuses to accept Weigert's idea as to the reasons for new growth after injury. This dictum of Weigert that such new growth is essentially repair due to the disturbing effect of a break in equilibrium, and not the direct effect of stimulation even in a minimal injury, has been very powerful among pathologists for years, and yet Dr. Adami presents the opposite views so forcibly that one can scarcely help wavering and finally accepting them. Doubtless there is much truth on both sides and Dr. Adami would be the last to maintain a narrow point of view. In speaking of tumors he considers the routine material adding only his plan of dividing tumors into "lepidic" and "hylic" according as they are derived from lining cells or from solid tissues. This, it seems, is merely a restatement of the idea which Hansemann first put forth and which has been in the minds of many, that probably it would be simpler and easier to give up the attempt to trace tissues back to their origins, and to content oneself with their adult form as a basis for their morphological classification so that a covering layer of cells without intercellular substance is, for Hansemann, epithelium no matter what its primary source, and tumors springing from it are named accordingly.

It seems of temporary importance at any rate to strive over these histogenetic questions with reference to tumors for the discovery of the etiological factors underlying the changes in the vital characters of the cells involved will surely render vain a great part of that.

The discussions of regressive tissue changes are especially good and the volume ends wtih their ultimate outcome—death.

As to the book itself, it may be said that the printing is good enough, the illustrations are fair—it is by no means richly illustrated and with the exception of diagrams and a few colored plates, nearly all, at least in the second volume, are from photographs. Literature references are given at times but they are not very complete nor always accurate—on page 384 volume 2 and page 445 volume 1, the work of Opie has been flatteringly but quite unfairly ascribed to the present reviewer.

On the whole there is no doubt that this is the best book on pathology in the English language. It brings forward all the usual material and discusses all the morbid processes and anatomical changes and the problems connected with them with eminent fairness, clearness and sanity. It errs perhaps a little as far as the mere medical student is concerned on the side of profusion and in theoretical discussion. It is not so much the work of a man whose mind is filled with the fresh pictures in all their colors, of the lesions he has just seen at the autopsy table, or with the movements of levers connected with the heart of his experimental animal, as that of the philosophic person who remembers these things and formulates clearly the explanations which are by no means so clear to the fresh observer.

Merck's Manual of the Materia Medica. Fourth Edition. (*Merck & Co.: New York, 1911.*)

This small pocket-book will be found useful by many practitioners. It is divided into four parts: 1, The Materia Medica as in actual use to-day by American Physicians; 2, Therapeutic Indications and Prescription Formulas for the use of the Materia Medica, and Bedside Diagnosis; 3, Classification of Medicaments; and 4, Miscellany. It is neatly prepared and can be safely recommended.

What Shall I Eat? By Dr. F. X. Gouraud. Translated by Francis J. Rebman. Price, $1.50. (*New York: Rebman Company. 1911.*)

It is rather difficult to know what view to express about this work for it is evidently intended both for the medical and general reader although it can hardly be regarded as satisfactory for either of them, which is generally the case in such works. Of the importance of proper diet there is no question, but it is

doubtful if this work gives much aid in deciding what is proper. The various forms of food are taken up in detail and the general composition stated. After this comes a statement of the effects of each article of food in particular diseases. There is everywhere a tendency to quote such varying opinions that one is frequently left in doubt as to what is really advised. On the much debated question of vegetarianism there is rather a good section in which the writer takes the view that it is by no means advisable for general application; it may be a good regimen for many but does not suit all.

There are a number of very curious statements here and there. Thus the opinion is quoted "that meat is not an aliment fit for the mind." Again meat is forbidden in "colonial diseases," whatever these may be. The author refers to a case of his own in which a man contracted typhoid fever "from eating a partridge that was too far advanced." Of course he did not contract typhoid fever from any such cause. He may have suffered from one of the forms of meat poisoning which sometimes resemble typhiod fever. In many places it is a little difficult to know what the author means, as when he says that "the arthritics form a family that disregards all restrictions as to diet with the utmost audacity." Then we find the statement that bread is a source of "humoral acidity," which sounds ominous but it is not easy to understand what is meant by this. Coffee is referred to as a "nerve food"; it certainly is rather a curious use of terms in a work devoted to a discussion of diet. The author condemns the drinking of water before or after eating but gives no reason for this sweeping statement. The probability is that many people are greatly aided by taking water before meals. Neither does he give any reason for the statement that ice water, or even cold water, is "ever harmful."

In the discussion of alcohol the following comment is made: "Normally alcohol acts through the kidneys. It is burned up there and eliminated in the form of water and carbonic acid." This certainly seems rather a curious statement. Then again alcohol is described as being a nervine and is stated to cause a "turmoil of excessive excitation, which is fatally followed by pronounced depression. . . . ." This succession of alternatives is said to lay the foundation for gastritis and cirrhosis of the liver.

That the book is intended for popular reading is shown by the inclusion of a glossary. It would have been well if this had been more carefully edited. Thus we find that atheroma is defined as a tumor. This is perhaps interesting as a guide to the derivation of the term but of course is not accurate in reference to its usage in this work or in medical writing.

We can not see that a book such as this is of any value. It is not likely that it will be of any special help to the members of the profession and certainly for the public it can not be regarded as a satisfactory guide. Take such a statement as this, "the habit of finishing every meal with a bit of cheese often enough proves fatal to men of the world." This suggests many questions which no doubt occur to the reader. Such a statement makes one distrust the writer of it as a good guide in matters of diet. Altogether the reading of this work will give the medical reader much more amusement than profit, but even so it can not be advised as worth the time.

A Practical Medical Dictionary. By THOMAS LATHROP STEDMAN, A. M., M. D. Illustrated. Price, $5. (*New York: William Wood & Co., 1911.*)

Dr. Stedman has had much experience in editing medical works, and this dictionary is at once an evidence of his learning and skill. It is, we believe, the best of its kind in the English language. Those interested in the origin of words will take especial satisfaction in using it, since, so far as possible, the editor has traced back each word to its source. Others will note with equal pleasure his effort to use correct derivatives, not hybrid words made from both Greek and Latin, but whenever possible a pure Greek or Latin word. Such efforts are however, as Dr. Stedman well recognizes, often vain. Take for example the word "appendicitis," which is a barbarism but it is so well established by use that there is no hope of changing it. Dr. Stedman shows that the proper term would be "scolecoiditis"; this sounds strange to our ears, but had it been as long in use as appendicitis, it would be no stranger to us than many surgical terms commonly used. Purity of language should be aimed at by all who wish to write correctly and this is all important in scientific language. Therefore this dictionary will be especially helpful to all medical authors.

What matter to admit in a dictionary and how it should be arranged (set up in type) are largely questions to be left to the editor's taste. Much is to be said in favor of the arrangement adopted by Dr. Stedman but as to the introduction of chemical terms and signs there may well be a difference of opinion. By admitting these Dr. Stedman has made his dictionary more complete than any other. His use of the Basle Anatomical Nomenclature is but another proof of the really scientific quality of the work. The proper selection of illustrations for any dictionary is always a puzzle but those found in this one may be said to be as satisfactory as in any.

The publishers as well as Dr. Stedman are to be congratulated in this new dictionary, which all medical writers will be glad to possess. The make-up of the volume is pleasing; the paper is good, the type excellent both in size and distinctness, so that with admirable spacing the use of the dictionary is made a pleasure.

Diseases of the Genito-Urinary Organs. By EDWARD L. KEYES, JR., M. D., Ph. D. Price, $6.00. (*New York: D. Appleton & Co., 1910.*)

This work of Keyes is probably one of the best that has so far been published for the general use of the student. The subject is dealt with clearly and concisely, yet at the same time thoroughly. The illustrations, which are found in profusion, are for the most part very good. The text is well written and makes very interesting reading.

The author has adapted the theory of Ciechanowski concerning the etiology of prostatic hypertrophy. This very attractive theory, which holds that chronic prostatitis is the direct cause of hypertrophy has, however, very little to support it from a statistical or pathological standpoint.

The value of the book is materially enhanced by the chapters on syphilis.

The volume as a whole is replete with practical information, and will prove to be a useful and valuable guide, not only to the general practitioner and student, but also to the specialist.

Prevention of Infectious Diseases. By ALVAH H. DOTY, M. D., Health Officer of the Port of New York. (*New York and London: D. Appleton & Co., 1911.*)

This little book of less than 300 pages is a valuable addition to the literature dealing with infectious diseases, expressing as it does the point of view of a health officer with many years' experience in this field. Such diseases as smallpox, yellow fever, typhus fever, plague and cholera are presented in detail from the sanitary standpoint, and the proper preventive measures to be employed in these diseases emphasized. The older theories which seek to account for the spread of infectious diseases by fomites, are contrasted with the newer theories in which the rôle of insects and bacillus carriers occupy a position of primary importance. The author is somewhat dogmatic in his treatment

of the subject, frequently expressing his personal individual opinion without giving his readers the facts and observations upon which his opinions are based. There is but little citation of authority, and a frequent and unnecessary repetition of statements of general import. The subjects of disinfection and disinfectants are particularly well handled. Despite a rather obstruse style and a general, rather than a special discussion of the subject matter, the book may be recommended to medical students interested in preventive medicine.

Die Faeces des Säuglings und des Kindes. Die Bedeutung Und Technik Ihrer Untersuchung. Von DR. ADOLF F. HECHT. Price, Mk. 8. (*Berlin und Wien: Urban & Schwarzenberg, 1910.*)

This monograph on the feces of infants and children treats in an exhaustive manner the composition of the feces in the norm and under pathological conditions, noting the significance of the result obtained thus far. The methods of the examination of the feces are given in such a manner as to render the book very valuable for workers in this field. The book is not only of value to the pediatrician but will be welcomed by the student of nutrition. S. A.

A Text-book of Bacteriology: A Practical Treatise for Students and Practitioners of Medicine. By PHILIP HANSON HISS, JR., M. D., Professor of Bacteriology, College of Physicians and Surgeons, Columbia University, New York City, and HANS ZINSSER, M. D., Professor of Bacteriology, Leland Stanford, Jr., University, Palo Alto, California. (*New York and London: D. Appleton & Co., 1910.*)

The appearance of a new text-book in any subject relating to the medical sciences is not usually a matter for congratulation, but the publication of a new treatise on bacteriology in 1910 by Dr. P. H. Hiss, Jr., Professor of Bacteriology in the Columbia University, New York, and Dr. Hans Zinsser, now Professor of Bacteriology in Leland Stanford, Jr., University, may be regarded in an entirely different light. In addition to a number of fairly mediocre text-books in this field which the American medical students have had to rely upon for some years, two publications of surpassing value have appeared within a comparatively short time, one the careful painstaking American edition of Muir and Ritchie by Harris, and the other the General Text-book of Bacteriology by E. O. Jordan, of the University of Chicago. Both of these books have been highly recommended to the readers of the BULLETIN. Hiss and Zinsser's work is thus the third of the really first-class books on this subject in English. It is far more comprehensive in its scope than either of those previously mentioned, and the reputation of its authors for scientific investigation of the highest character is at once a guarantee of the excellence of the work. We have now been able to utilize this text-book in teaching two classes in bacteriology and our experience in its use has only fulfilled the highest expectations formed originally. Throughout the whole volume a strong conservative tone is manifest. Facts are not accepted without due evidence, doubt is always expressed when the opportunity for doubt exists, and allowance is always made for the various interpretations which can be drawn from reported observations.

The book consists of over 700 pages divided into 54 chapters. These chapters are grouped under five different sections. Section I deals with the General Biology of Bacteria and the Technique of Bacteriological Study, Section II with Infection and Immunity, Section III with Pathogenic Microorganisms, Section IV with Diseases of Unknown Etiology, and Section V with Bacteria in Air, Soil, Water and Milk. In the first section the historical side of the subject is well presented but possibly too concisely for a work so pretentious as this and in our opinion the great and fundamental value of Koch's early work on bacteria is not properly indicated. It was Koch's work on anthrax in 1876 that began a new era in bacteriology, and his discovery of the tubercle bacillus and the cholera vibrio that directed the attention of the medical public to this field. The chapters devoted to the biological activities of bacteria are clearly written, and in those dealing with microscopic study and staining methods, and with the preparation of cultural media, there is a wealth of detail gratifying alike to instructor and student.

In Section II on Infection and Immunity nearly one hundred and fifty pages are devoted to the subject and nearly every phase of it is considered. Toxins, antitoxins, lysins, agglutinins, precipitins, opsonins, aggressins, and anaphylaxis are all considered in detail. The theories of immunity are presented with great clarity and are not too much amplified. Especial emphasis is laid upon the technique of serum reactions, material rarely presented in text-books and upon the practical bearing of the facts and problems of immunity upon the science of medicine.

Section III is devoted to the Pathogenic Microorganisms which affect man. They are described with great accuracy and the lesions with which they are associated in man and which they produce in animals are carefully portrayed. Especially to be praised is the description of the cultural reactions of such organisms as the pneumococcus and streptococcus, the typhoid bacillus and the dysentery bacillus. In this section the authors have made no particular attempt to apply correct botanical names. This may be regarded as an unwise procedure from a scientific standpoint, but possibly justified in a text-book written primarily for students of medicine. The chapter on the leprosy bacillus was evidently prepared before the work on this organism by Clegg in the Philippine Islands and Duval in New Orleans, although the book apparently went to press after the important investigations of these authors had come to light. This is extremely unfortunate since it renders a thorough revision of this chapter necessary and fails in its present form to give any credit to investigators who have succeeded in cultivating organisms which have defied the attempts of some of the foremost men in the field of bacteriology. Another achievement of American workers, the solution of the etiology of hog cholera, is not presented, but this may be excused on the plea that this text-book is devoted to the organisms which infect man. The value of this work, however, and the relation of the fact brought out by Dorset, McBride and Bolton, that hog cholera is due to a filterable virus, to problems of infection in man and to the general subject of immunity, might have been made an excuse for reporting in detail what we must regard as one of the greatest contributions of American bacteriologists.

In Section IV, devoted to Diseases of Unknown Etiology and Section V, on Bacteria in Air, Soil, Water and Milk, the main points of importance in this connection are presented clearly and concisely.

The book is highly to be commended both to the medical student and the practicing physician. From the standpoint of the instructor it satisfies a need long felt in teaching the subject of bacteriology, and will, we believe, become one of our most popular text-books on this subject. W. W. FORD.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Subscriptions, $2.00 a year (foreign postage, 50 cents), may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each. Single copies may also be procured from the BALTIMORE NEWS CO., Baltimore.